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As submitted confidentially with the Securities and Exchange Commission on June 25, 2014. This draft registration statement has not been publicly filed with the Securities and Exchange Commission and all information herein remains strictly confidential.

Registration No. 333-

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# UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

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## FORM S-1

REGISTRATION STATEMENT  
Under  
The Securities Act of 1933

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### Proteon Therapeutics, Inc.

(Exact name of Registrant as specified in its charter)

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<b>Delaware</b> (State or Other Jurisdiction of Incorporation or Organization)	<b>2836</b> (Primary Standard Industrial Classification Code Number)	<b>20-4580525</b> (I.R.S. Employer Identification Number)
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**200 West Street  
Waltham, MA 02451  
(781) 890-0102**

(Address, including zip code, and telephone number, including area code, of Registrant's principal executive offices)

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**Timothy P. Noyes  
Chief Executive Officer  
Proteon Therapeutics, Inc.  
200 West Street  
Waltham, MA 02451  
(781) 890-0102 x1021**

(Name, address, including zip code, and telephone number, including area code, of agent for service)

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**Approximate date of commencement of the proposed sale to the public:** As soon as practicable after the effective date of this Registration Statement.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act, check the following box.

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering.

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of "large accelerated filer," "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer

Accelerated filer

Non-accelerated filer   
(Do not check if a  
smaller reporting company)

Smaller reporting company

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CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Proposed Maximum Aggregate Offering Price(1)(2)	Amount of Registration Fee
Common Stock, \$0.001 par value per share	\$	\$

- (1) Includes additional shares of common stock that the underwriters have the option to purchase.
- (2) Estimated solely for the purpose of calculating the registration fee pursuant to Rule 457(o) under the Securities Act of 1933, as amended.

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933, as amended, or until the Registration Statement shall become effective on such date as the Securities and Exchange Commission, acting pursuant to said Section 8(a), may determine.

The information in this preliminary prospectus is not complete and may be changed. These securities may not be sold until the registration statement filed with the Securities and Exchange Commission is effective. This preliminary prospectus is not an offer to sell these securities and we are not soliciting offers to buy these securities in any jurisdiction where the offer or sale is not permitted.

**SUBJECT TO COMPLETION, DATED JUNE 25, 2014**

**PRELIMINARY PROSPECTUS**



**Shares**

**Common Stock**

**\$ per share**

This is the initial public offering of Proteon Therapeutics, Inc. We are offering \_\_\_\_\_ shares of our common stock. Prior to this offering, there has been no public market for our common stock. We estimate that the initial public offering price of our common stock will be between \$ \_\_\_\_\_ and \$ \_\_\_\_\_ per share.

We intend to apply to have our common stock listed on The NASDAQ Global Market under the symbol "PRTO."

We are an "emerging growth company" as that term is used in the Jumpstart Our Business Startups Act of 2012 and, as such, we have elected to comply with certain reduced public company reporting requirements for this prospectus and future filings.

**Investing in our common stock involves risks. See "Risk Factors" beginning on page 13.**

	<b>Per Share</b>	<b>Total</b>
Initial public offering price	\$ _____	\$ _____
Underwriting discount and commissions(1)	\$ _____	\$ _____
Proceeds, before expenses, to us	\$ _____	\$ _____

(1) We have agreed to reimburse the underwriters for certain expenses. See "Underwriting."

We have granted the underwriters a 30-day option to purchase up to a total of \_\_\_\_\_ additional shares of common stock on the same terms and conditions set forth above.

The underwriters expect to deliver the shares of common stock to purchasers on \_\_\_\_\_, 2014.

*Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.*

**Stifel**

**Baird**

**JMP Securities**

**Oppenheimer & Co.**

The date of this prospectus is \_\_\_\_\_, 2014

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Unless the context requires otherwise, references in this prospectus to "Proteon," "the Company," "we," "us" and "our" refer to Proteon Therapeutics, Inc.

In this prospectus, we refer to our subsidiary Proteon Therapeutics Limited as "Proteon UK."

You should rely only on the information contained in this prospectus or contained in any free writing prospectus filed with the Securities and Exchange Commission. Neither we nor the underwriters have authorized anyone to provide you with additional information or information different from that contained in this prospectus or in any free writing prospectus filed with the Securities and Exchange Commission. We are offering to sell, and seeking offers to buy, our common stock only in jurisdictions where offers and sales are permitted. The information contained in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus, or of any sale of our common stock.

**Through and including \_\_\_\_\_, 2014 (the 25th day after the date of this prospectus), all dealers that effect transactions in these securities, whether or not participating in this offering, may be required to deliver a prospectus. This is in addition to the dealers' obligation to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.**

For investors outside the United States: Neither we nor any of the underwriters have done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than in the United States. You are required to inform yourselves about and to observe any restrictions relating to this offering and the distribution of this prospectus outside of the United States.

## PROSPECTUS SUMMARY

*This summary highlights information contained elsewhere in this prospectus and does not contain all the information that you should consider in making your investment decision. You should read the entire prospectus, including our financial statements and related notes and the information set forth in the sections titled "Risk Factors," "Special Note Regarding Forward-Looking Statements" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" before deciding whether to purchase shares of our common stock. Unless the context otherwise requires, we use the terms "Proteon," "our company," "we," "us" and "our" in this prospectus to refer to Proteon Therapeutics, Inc.*

### Company Overview

We are a late-stage biopharmaceutical company focused on the development of novel, first-in-class pharmaceuticals to address the needs of patients with renal and vascular disease. Our product candidate, PRT-201, is a recombinant human elastase that we are developing to reduce vascular access failure in patients with chronic kidney disease undergoing or preparing for hemodialysis, a lifesaving treatment that cannot be conducted without a functioning vascular access. We believe the data from our completed Phase 2 trial of PRT-201 in patients undergoing creation of an arteriovenous fistula, or AVF, support that a one-time, local application of PRT-201 during AVF surgical placement reduces AVF failure, thereby improving patient outcomes and reducing the burden on patients and the healthcare system. We are not aware of any approved preventative treatments to reduce the failure rate of AVFs.

In May 2014, following the results from our Phase 2 trial and to fund our first Phase 3 trial, we closed on the \$25.0 million first tranche of a \$45.0 million total financing. The financing was led by Abingworth, Deerfield and Pharmstandard and included investments from our existing venture investors. We expect to initiate the first of two Phase 3 trials for PRT-201 in radiocephalic AVFs, our initial indication, in the third quarter of 2014 and initiate the second Phase 3 trial in the first half of 2015. PRT-201 has received fast track designation from the United States Food and Drug Administration, or FDA, and orphan drug designation in the United States and European Union, for hemodialysis vascular access indications.

We retain worldwide commercial rights to PRT-201. If approved by regulatory authorities, we intend to commercialize this product in the United States ourselves with a specialty hospital sales force, focused primarily on vascular surgeons, and intend to seek one or more collaborators to commercialize the product in additional markets. Our patents include claims covering formulations, methods of manufacturing and uses of elastases, providing protection in the United States and European Union through 2028, and with potential extension through 2032 in the United States.

### Established Medical Need

The need to improve vascular access outcomes is well established in the hemodialysis community. A 2014 publication estimated the total cost of managing hemodialysis vascular access dysfunction in the United States to be approximately \$2.9 billion annually. AVFs are the gold standard of vascular access for hemodialysis as they are associated with fewer complications and reduced rates of hospitalization. However AVFs have a greater than 50% failure rate in their first year after surgical placement, resulting in frequent surgical or interventional procedures and a high rate of abandonment, leading to increased morbidity, mortality and costs of care.

We estimate there are approximately 130,000 AVFs created in the United States annually. In an AVF procedure a surgeon transects a vein and sutures it to the side of a nearby artery, typically in the arm. There are a limited number of potential artery-vein combinations in the arm that can be used by surgeons to create an AVF. The medical community endorses radiocephalic AVFs, in which the cephalic vein is sutured to the radial artery in the wrist, as the optimal form of vascular access and the recommended first choice for new hemodialysis patients. A radiocephalic AVF as compared to other forms of vascular access preserves the potential future use of other access further up in the arm, is simpler to create and is less

likely to result in serious complications, including heart failure, central stenosis, which is the narrowing of blood vessels in shoulder or chest, and reduced blood flow to the hand. Unfortunately, radiocephalic AVFs suffer from high failure rates, with up to 70% failing within 12 months after their surgical placement. We estimate that approximately 40% of all AVF placements are radiocephalic.

While AVF failure can usually be restored via an intervention such as balloon angioplasty, which is dilation of a blood vessel with a balloon, or a surgical revision. However, these procedures are costly, invasive, painful, and associated with a number of complications and often need to be repeated. AVF patients in the United States on average require greater than 1.5 procedures per year. Procedures to restore function typically cost Medicare between \$5,000 and \$13,000 per procedure. A recent publication indicates that maintaining a radiocephalic AVF can cost on average more than \$17,000 in the first year after surgical placement.

## **PRT-201**

We demonstrated that PRT-201, a recombinant human elastase, generates fragments of elastin, a protein present in blood vessel walls. We believe the fragments of elastin inhibit formation of neointimal hyperplasia, which is the growth of tissue inside vessels that narrows AVFs and reduces blood flow. We believe that a one-time local application of PRT-201 to the external surface of the vessels during AVF surgical placement can modify the injury response, or scarring, resulting from surgery and thereby reduce the severity of neointimal hyperplasia and AVF failure following surgery. We believe that, if our Phase 3 clinical program is successful, PRT-201 will potentially become the standard of care for patients with chronic kidney disease who are undergoing surgical placement of a radiocephalic AVF.

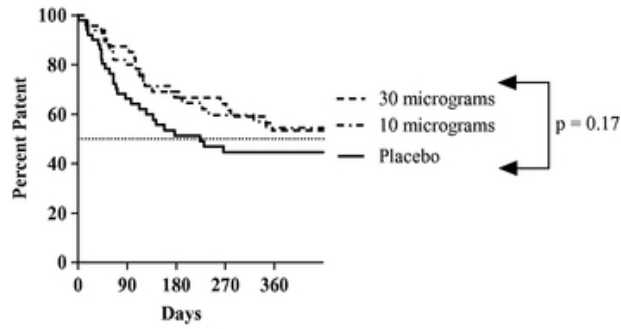
### ***Phase 2 AVF Trial Results***

In 2013, we completed a multicenter, randomized, double-blind, placebo-controlled Phase 2 trial of PRT-201, which treated 151 patients with chronic kidney disease undergoing surgical creation of a radiocephalic AVF (n=67) or brachiocephalic AVF (n=84), which is performed by suturing the brachial artery to the cephalic vein at the elbow. Of these 151 patients, 51 patients received placebo, 51 patients received a dose of 10 micrograms of PRT-201, and 49 patients received a dose of 30 micrograms of PRT-201. The primary efficacy endpoint was AVF primary unassisted patency, defined as the time from surgical creation of the AVF to occurrence of a thrombosis or an intervention, such as angioplasty to restore or maintain patency, or function. Other efficacy endpoints included unassisted maturation, which is defined as increase in vessel diameter and blood flow at the AVF without the need for an intervention such as angioplasty, average rate of procedures to restore or maintain AVF patency, secondary patency, which is defined as abandonment of the AVF and the need for creation of a new vascular access, use for hemodialysis and hemodynamically significant stenosis, or narrowing of blood vessels.

#### ***Primary Endpoint***

Both doses of PRT-201 showed a trend toward efficacy, although neither dose met the primary endpoint with statistical significance. Median patency, the time at which 50% of patients in a group lost primary unassisted patency, was 224 days in the placebo group and greater than 365 days in each of the PRT-201 treatment groups, indicating that PRT-201 prolonged primary unassisted patency. The following Kaplan-Meier curves display primary unassisted patency.

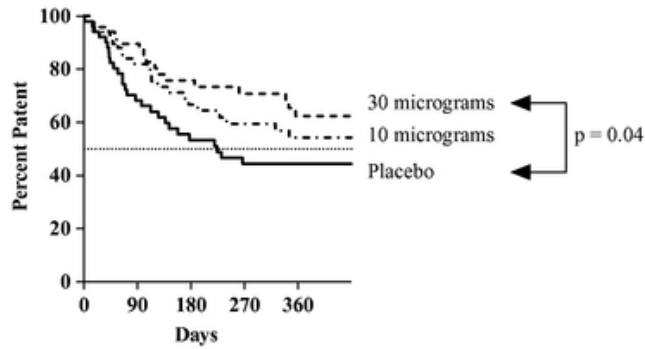
**Primary Unassisted Patency—All AVFs**



Note: Prespecified analysis.

An analysis of the primary endpoint data revealed an uneven distribution in primary unassisted patency loss events due to central stenosis, which occur remote from the site of an AVF. Central stenoses commonly exist prior to AVF placement and are unrelated to treatment with PRT-201. Therefore, to correct for this uneven distribution, we conducted a non-prespecified analysis of the primary endpoint that excluded patency loss events due to central stenoses. The following Kaplan-Meier curves display primary unassisted patency for all AVFs (excluding central stenoses), suggesting a reduction in the risk of primary unassisted patency loss ( $p=0.04$ , for the 30 microgram dose versus placebo).

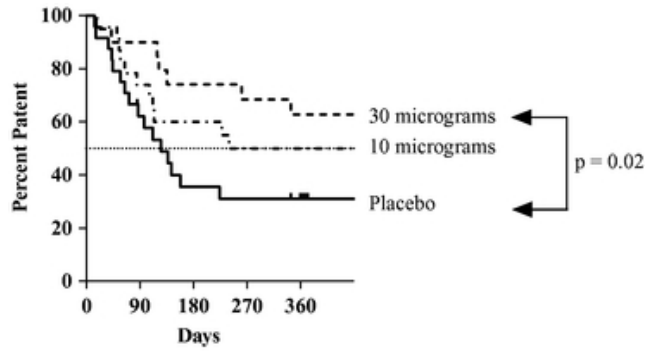
**Primary Unassisted Patency—All AVFs  
(Excluding Central Stenoses)**



Note: Not prespecified analysis.

The benefit of PRT-201 on primary unassisted patency was most pronounced in the subset of patients undergoing placement of a radiocephalic AVF. Recent publications indicate that radiocephalic AVFs suffer from higher rates of patency loss and maturation failure, with up to 70% of AVFs in the wrist being subject to patency loss within 12 months after their surgical placement. The subset analysis of this endpoint was not prespecified. The following Kaplan-Meier curves display the reduction in risk of primary unassisted patency loss in the subset of patients with radiocephalic AVFs. Median patency was 125 days in the placebo group and greater than 365 days in the 30 microgram group, indicating an improvement in primary unassisted patency ( $p=0.02$ , for the 30 microgram dose versus placebo).

**Primary Unassisted Patency—Radiocephalic AVFs**



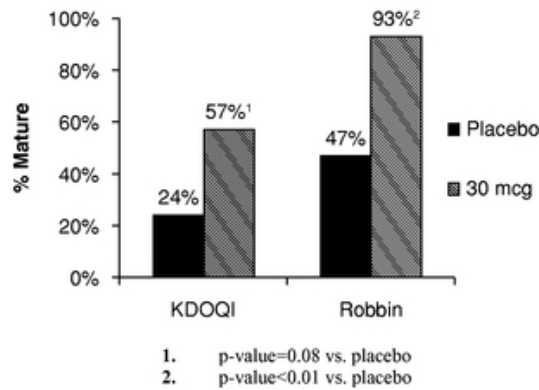
Note: Not prespecified analysis.

*Secondary Endpoints*

In one of our prespecified secondary endpoints, unassisted maturation, which is defined as adequate vessel diameter and blood flow without the need for intervention such as angioplasty, PRT-201 showed a significant benefit at three months in the 30 microgram dose using the two commonly accepted measures of maturation, namely, the Robbin criteria ( $p < 0.01$ ) and the KDOQI criteria ( $p = 0.03$ ).

The effect of PRT-201 on maturation was more pronounced in the subset of patients who underwent creation of a radiocephalic AVF. For the 30 microgram dose of PRT-201, unassisted maturation of the radiocephalic AVF, a prespecified analysis, showed an increase in the percentage of patients with mature AVFs compared with placebo using the Robbin criteria ( $p < 0.01$ ) and a trend toward improvement using the KDOQI criteria ( $p = 0.08$ ).

**Unassisted Maturation—Radiocephalic AVFs**



Note: Prespecified analysis.

*Safety and Tolerability*

In the trial, patients treated with PRT-201 reported adverse events comparable to placebo. These events were consistent with the medical events experienced by chronic kidney disease patients undergoing AVF placement surgery. The most common adverse events were AVF incision pain, venous stenosis, AVF thrombosis, steal syndrome and hypoesthesia. Serious adverse events, or SAEs, reported by the investigator as possibly drug-related occurred in two 10 microgram PRT-201 patients, both AVF thrombosis, and two 30 microgram patients (one chest pain and one swelling at the surgical incision). There were no SAEs reported by the investigator as possibly drug-related in the placebo group. There was one SAE reported by the investigator to be drug-related in the 10 microgram PRT-201 group, AVF maturation failure, and there were none in the other treatment groups.



### **Phase 3 Trial Design**

In April 2013, we held an end of Phase 2 meeting with the FDA during which we confirmed elements of our Phase 3 development plan, including the primary endpoint. We plan to perform two Phase 3 trials of PRT-201 using a 30 microgram dose, enrolling patients undergoing surgical placement of a radiocephalic AVF. In our Phase 2 trial, PRT-201 showed the greatest benefit in radiocephalic AVFs.

The Phase 3 trials will use the same primary endpoint, primary unassisted patency over 12 months, used in our Phase 2 trial. In our end of Phase 2 meeting with the FDA, the FDA agreed that primary unassisted patency could be used as the primary endpoint. Our secondary endpoint, secondary patency over 12 months, and tertiary endpoints, unassisted maturation, use for hemodialysis and average procedure rates, in our Phase 3 trials were all endpoints in our Phase 2 trial.

We plan to begin enrolling patients in our first 300 patient Phase 3 clinical trial in the third quarter of 2014, and anticipate that results will be available in 2017. The Phase 3 clinical trial will include two groups, one receiving PRT-201 (n=200) and the other receiving placebo (n=100). We expect to initiate the second, substantial similar, Phase 3 clinical trial in the first half of 2015. If the results of the first Phase 3 trial are sufficiently compelling, we intend to meet with the FDA to discuss the possibility of submitting a Biologics License Application, or BLA, supported by the single Phase 3 trial and may decide to submit a BLA to the FDA prior to completing the second Phase 3 trial.

### **Additional PRT-201 Indications**

We believe that PRT-201 has potential benefits for hemodialysis patients undergoing other types of vascular access procedures. In 2013, we completed a successful Phase 1/2 trial in patients undergoing surgical placement of an arteriovenous graft, or AVG, which is a synthetic tube a surgeon uses to connect a vein and an artery. We may develop PRT-201 for additional hemodialysis indications including AVGs or brachiocephalic AVFs.

We believe PRT-201 also has the potential to treat a number of renal and vascular diseases for which therapeutic options are limited. We are currently enrolling patients with symptomatic peripheral artery disease, or PAD, in a Phase 1 dose-escalation trial in which patients are treated with PRT-201 via a drug delivery catheter following balloon angioplasty.

### **Commercial Opportunity**

We estimate approximately 130,000 AVFs are created in the United States annually, of which 40% are radiocephalic. We believe that the number of radiocephalic AVFs created annually may rise significantly if PRT-201 gains FDA approval, as this would allow surgeons to place radiocephalic AVFs in patients that they previously considered at an unacceptably high risk of AVF failure.

If approved, PRT-201 will be administered primarily by vascular surgeons, who we believe are acutely aware of the clinical need and are receptive to new therapies. We believe PRT-201 will be reimbursed appropriately as costs related to AVF surgical placement, which is typically performed in the hospital outpatient setting, are not included in the ESRD bundle, the single bundled payment from Medicare for a number of the costs of hemodialysis treatments, medications, labs and supplies for patients with end stage renal disease. We believe that PRT-201 adoption will be supported by key stakeholders, including referring nephrologists, patient advocacy groups, large dialysis organizations and payors. We plan to target our marketing and sales efforts to vascular surgeons who create AVFs. There are approximately 2,800 vascular surgeons in the United States. We believe a specialty hospital sales force of approximately 75-100 representatives will enable us to call on the approximately 1,300 hospitals that account for more than 90% of the AVF surgical placements performed in the United States annually.

## Our Strengths

We believe our company and PRT-201 possess the following attributes that increase the likelihood that we will be successful in developing and commercializing PRT-201:

- *Entering Phase 3 trials for radiocephalic AVF placement.* We plan to conduct our Phase 3 clinical trials in radiocephalic AVFs using a 30 microgram dose of PRT-201, the population and dose in which, in a non-prespecified analysis, we observed an improvement in primary unassisted patency with PRT-201 in our Phase 2 trial.
- *Phase 3 endpoints same as our Phase 2 trial.* The primary endpoint in our Phase 3 trial, primary unassisted patency, will be the same as that used in our Phase 2 trial. In April 2013, we held an end of Phase 2 meeting with the FDA during which we confirmed elements of our Phase 3 development plan including the primary endpoint.
- *Safety profile supports approval.* Based on results from our clinical trials and preclinical studies, we believe PRT-201, which is administered once and only acts locally, has demonstrated a safety profile that will support approval if our planned Phase 3 clinical program is successful. At our end of Phase 2 meeting with the FDA, we confirmed that we do not need to conduct any additional preclinical studies to support a BLA filing.
- *Unmet medical need.* A 2014 publication estimated the total cost of managing hemodialysis vascular access dysfunction in the United States to be approximately \$2.9 billion annually. We are not aware of any approved preventative treatments to reduce the AVF failure rate. PRT-201 has received fast track designation from the FDA, which expedites the development of drugs to treat serious conditions and fill an unmet medical need.
- *Substantial and readily-addressable market opportunity.* We estimate a sales force of approximately 75-100 representatives will enable us to call on the approximately 1,300 hospitals that account for more than 90% of the AVF surgical placements performed in the United States annually. We believe PRT-201 will be reimbursed adequately as costs related to AVF surgical placement, which is typically performed in the hospital outpatient setting, are not included in the ESRD bundle.
- *Experienced team.* Both our Chief Executive Officer and Chief Medical Officer were senior executives at GelTex, a biopharmaceutical company, where they played leading roles in the development and commercialization of Renagel, a treatment for hemodialysis patients that led to Genzyme's acquisition of GelTex for more than \$1 billion.

## Our Strategy

Our strategy is to develop and commercialize PRT-201 for patients suffering from renal and vascular diseases, beginning with patients undergoing surgical creation of a radiocephalic AVF. Key elements of our strategy include our plans to:

- complete clinical development of PRT-201 and seek regulatory approval in its lead indication in the United States;
- commercialize PRT-201 directly in the United States;
- undertake clinical development of PRT-201 in Europe and establish partnerships for commercialization of PRT-201 in all or parts of Europe;
- pursue additional indications for PRT-201;
- establish partnerships for development and commercialization of PRT-201 in Japan and other Asian countries; and
- in-license or acquire additional product opportunities.

## **Risks Associated with Our Business**

Our business is subject to numerous risks and uncertainties, including those highlighted in the section entitled "Risk Factors" immediately following this prospectus summary. These risks include, among others, the following:

- we have a limited operating history and have incurred significant losses since our inception and we anticipate that we will continue to incur losses for the foreseeable future;
- we will require substantial additional financing to achieve our goals, and failure to obtain this necessary capital when needed on acceptable terms, or all, could force us to delay, limit, reduce or terminate our product development, any commercialization efforts or other operations;
- we are substantially dependent on the success of our current product candidate, PRT-201, and cannot guarantee that this product candidate will successfully complete Phase 3 clinical trials, receive regulatory approval or be successfully commercialized;
- PRT-201 may not have favorable results in later clinical trials or receive regulatory approval;
- the denial or delay of regulatory approval of PRT-201 or any additional product candidates would prevent or delay commercialization and have a material adverse effect on our potential to generate revenue, our business and our results of operations;
- if we are unable to establish effective marketing and sales capabilities or enter into agreements with third parties to market and sell our product candidates, if they are approved, we may be unable to generate product revenues;
- even if PRT-201 or any additional product candidates receive regulatory approval, they may fail to achieve the broad degree of physician adoption necessary for commercial success;
- PRT-201 or any additional product candidates, if approved, may face significant competition and our failure to effectively compete may prevent us from achieving significant market penetration and expansion;
- we and our contract manufacturers are subject to significant regulation with respect to manufacturing our product candidates. The manufacturing facilities on which we rely may not continue to meet regulatory requirements and have limited capacity; and
- if our efforts to protect our intellectual property related to PRT-201 or any additional product candidates are not adequate, we may not be able to compete effectively in our market.

## **Corporate Information**

Proteon was incorporated under the laws of the State of Delaware in March 2006, and at that time, acquired Proteon Therapeutics, LLC, our predecessor, which was formed in June 2001. Our executive offices are located at 200 West Street, Waltham, Massachusetts 02451, and our telephone number is (781) 890-0102. Our website address is [www.ProteonTherapeutics.com](http://www.ProteonTherapeutics.com). The information contained on, or accessible through, our website does not constitute part of this prospectus. We have included our website address in this prospectus solely as an inactive textual reference.

## **Implications of Being an Emerging Growth Company**

We are an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012. We will remain an emerging growth company until the earlier of (1) the last day of the fiscal year (a) following the fifth anniversary of the completion of this offering, (b) in which we have total annual gross revenue of at least \$1.0 billion, or (c) in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds \$700 million as of the prior June 30th, and (2) the date on which we have issued more than \$1.0 billion in non-convertible debt securities during the prior three-year period. We refer to the Jumpstart Our Business Startups Act of 2012 in this prospectus as the "JOBS Act," and references in this prospectus to "emerging growth company" shall have the meaning ascribed to it in the JOBS Act.

As an emerging growth company, we may take advantage of specified reduced disclosure and other requirements that are otherwise applicable, in general, to public companies that are not emerging growth companies. These provisions include:

- reduced disclosure about our executive compensation arrangements;
- exemption from the non-binding shareholder advisory votes on executive compensation or golden parachute arrangements;
- exemption from the auditor attestation requirement in the assessment of our internal control over financial reporting; and
- reduced disclosure of financial information in this prospectus, such as being permitted to include only two years of audited financial information and two years of selected financial information in addition to any required unaudited interim financial statements, with correspondingly reduced "Management Discussion and Analysis of Financial Condition and Results of Operations" disclosure.

We may choose to take advantage of some, but not all, of the available exemptions. We have taken advantage of some reduced reporting burdens in this prospectus. Accordingly, the information contained herein may be different than the information you receive from other public companies in which you hold stock. The JOBS Act permits an emerging growth company to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies. We have irrevocably elected not to avail ourselves of this extended transition period and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for non-emerging growth companies.

## THE OFFERING

Common stock we are offering	shares
Common stock outstanding after giving effect to this offering	shares
Option to purchase additional shares	The underwriters have a 30-day option to purchase a total of additional shares of common stock.
Use of proceeds	We estimate that our net proceeds from this offering will be approximately \$ million at an assumed initial public offering price of \$ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. We expect to use the net proceeds of this offering to accelerate the commencement of our second Phase 3 clinical trial of PRT-201, to accelerate our chemistry and manufacturing controls activities, to fund additional research and development activities and for other general corporate purposes. See "Use of Proceeds."
Risk factors	See "Risk Factors" beginning on page 13 and the other information included in this prospectus for a discussion of factors you should carefully consider before deciding to invest in our common stock.
Proposed NASDAQ Global Market Symbol	"PRTO"

In this prospectus, unless otherwise indicated, the number of shares of common stock outstanding and the other information based thereon is based on shares of common stock outstanding as of March 31, 2014 and does not reflect:

- 9,629,620 shares of common stock issuable upon exercise of stock options outstanding as of March 31, 2014 at a weighted-average exercise price of \$0.14 per share;
- 10,471,282 shares of our common stock issuable upon exercise of warrants with a weighted-average exercise price of \$0.29 per share that we expect to be exercised prior to the closing of this offering;
- 255,504 shares of common stock reserved for issuance pursuant to future equity awards under our 2006 Equity Incentive Plan; and
- shares of common stock reserved for future issuance under our 2014 Equity Incentive Plan, which will become effective immediately prior to the closing of this offering (including shares of common stock reserved for issuance under our 2006 Equity Incentive Plan, which will be added to the shares reserved under the 2014 Equity Incentive Plan upon its effectiveness).

Unless otherwise indicated, all information in this prospectus reflects or assumes the following:

- the amendment and restatement of our certificate of incorporation and bylaws, which will occur immediately prior to the closing of this offering;
- the conversion of all of our outstanding shares of our preferred stock into 67,504,949 shares of common stock, including the conversion of our Series convertible preferred stock on an assumed one-for-one basis which will occur automatically upon the closing of this offering. See

"Capitalization—Series D Convertible Preferred Stock" for applicable conversion price adjustments;

- a one-for- reverse stock split of our common stock to be effected on , 2014 prior to completion of this offering;
- no exercise of stock options on or after March 31, 2014; and
- no exercise by the underwriters of their option to purchase up to a total of additional shares of common stock in this offering.

**SUMMARY FINANCIAL DATA**

The following summary financial data for the years ended December 31, 2012 and 2013 have been derived from our audited financial statements included elsewhere in this prospectus. The selected statement of operations data for the three months ended March 31, 2013 and 2014 and the selected balance sheet data as of March 31, 2014 were derived from our unaudited financial statements appearing elsewhere in this prospectus. These unaudited financial statements have been prepared on a basis consistent with our financial statements and, in our opinion, contain all adjustments, consisting only of normal and recurring adjustments, necessary for a fair presentation of such financial data. You should read this data together with our audited financial statements and related notes included elsewhere in this prospectus for the information under the captions "Selected Financial Data" and "Management's Discussion and Analysis of Financial Condition and Results of Operations." Our historical results are not necessarily indicative of our future results, and our operating results for the three-month period ended March 31, 2014 are not necessarily indicative of the results that may be expected for the fiscal year ending December 31, 2014 or any other interim periods or any future year or period.

	<u>Years Ended December 31,</u>		<u>Three Months Ended</u>	
	<u>2012</u>	<u>2013</u>	<u>March 31,</u>	<u>2014</u>
			<u>(unaudited)</u>	
	<u>(in thousands, except share and per share data)</u>			
<b>Statement of Operations Data:</b>				
Operating expenses:				
Research and development	\$ 5,907	\$ 3,994	\$ 1,134	\$ 1,189
General and administrative	2,089	3,128	737	744
Total operating expenses	<u>7,996</u>	<u>7,122</u>	<u>1,871</u>	<u>1,933</u>
Loss from operations	(7,996)	(7,122)	(1,871)	(1,933)
Other income (expense):				
Investment income	20	4	2	—
Interest expense	—	(861)	—	(828)
Other income (expense)	6	67	4	(70)
Total other income (expense)	<u>26</u>	<u>(790)</u>	<u>6</u>	<u>(898)</u>
Net loss	<u>(7,970)</u>	<u>(7,912)</u>	<u>(1,865)</u>	<u>(2,831)</u>
Unrealized loss on available-for-sale investments	(5)	(1)	—	—
Comprehensive loss	<u>\$ (7,975)</u>	<u>\$ (7,913)</u>	<u>\$ (1,865)</u>	<u>\$ (2,831)</u>
Reconciliation of net loss to net loss attributable to common stockholders				
Net loss	\$ (7,970)	\$ (7,912)	\$ (1,865)	\$ (2,831)
Accretion of redeemable convertible preferred stock to redemption value	(6,133)	(6,119)	(1,512)	(1,512)
Net loss attributable to common stockholders	<u>\$ (14,103)</u>	<u>\$ (14,031)</u>	<u>\$ (3,377)</u>	<u>\$ (4,343)</u>
Net loss per share attributable to common stockholders—basic and diluted(1)	<u>\$ (3.85)</u>	<u>\$ (3.76)</u>	<u>\$ (0.92)</u>	<u>\$ (1.14)</u>
Weighted-average number of common shares used in net loss per share attributable to common stockholders—basic and diluted(1)				
	<u>3,659,790</u>	<u>3,732,436</u>	<u>3,659,790</u>	<u>3,811,014</u>
Pro forma net loss per share attributable to common stockholders—basic and diluted (unaudited)(1)(2)	<u>\$ (0.10)</u>		<u>\$ (0.03)</u>	
Pro forma weighted-average number of common shares used in net loss per share attributable to common stockholders—basic and diluted (unaudited)(1)(2)				
	<u>72,457,068</u>		<u>75,186,284</u>	

	As of March 31, 2014	
	Actual	Pro Forma As Adjusted(3)(4)(5) (unaudited) (in thousands)
<b>Balance Sheet Data:</b>		
Cash and cash equivalents	\$ 3,586	\$ 3,586
Working capital	(6,978)	(930)
Total assets	4,045	4,045
Preferred stock	97,917	—
Common stock and additional paid in capital	4	102,457
Total stockholders' deficit	(104,840)	(875)

- (1) See Note 2 within the notes to our financial statements appearing elsewhere in this prospectus for a description of the method used to calculate basic and diluted net loss per common share and pro forma basic and diluted net loss per common share.
- (2) Pro forma to reflect the conversion of all outstanding shares of our preferred stock into shares of common stock upon the closing of this offering.
- (3) Pro forma as adjusted to reflect the pro forma adjustments described in (2) above, and to further reflect (i) the filing and effectiveness of our amended and restated certificate of incorporation, which will occur immediately prior to the closing of this offering and (ii) the sale of shares of our common stock offered in this offering, assuming an initial public offering price of \$ per share, the midpoint of the price range set forth on the cover page of this prospectus, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.
- (4) A \$1.00 increase (decrease) in the assumed initial public offering price of \$ per share, the midpoint of the price range set forth on the cover of this prospectus, would increase (decrease) the pro forma as adjusted amount of each of cash and cash equivalents, working capital, total assets, common stock and additional paid-in-capital and total stockholders' deficit by approximately \$ million, assuming that the number of shares offered by us, as set forth on the cover of this prospectus, remains the same and after deducting underwriting discounts and commissions and estimated offering expenses payable by us.
- (5) A 1,000,000 share increase in the number of shares offered by us together with a concomitant \$1.00 increase in the assumed initial public offering price of \$ per share, the midpoint of the price range set forth on the cover of this prospectus, would increase the pro forma as adjusted amount of each of cash and cash equivalents, and total stockholders' deficit by approximately \$ million, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.



## RISK FACTORS

*Investing in our common stock involves a high degree of risk. You should carefully consider the risks and uncertainties described below, together with all of the other information in this prospectus, including our financial statements and related notes, before deciding whether to purchase shares of our common stock. If any of the following risks are realized, our business, operating results and prospects could be materially and adversely affected. In that event, the price of our common stock could decline, and you could lose part or all of your investment. The risks and uncertainties described below are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently believe to be immaterial may also adversely affect our business.*

### **Risks Related to Our Financial Condition and Need for Additional Capital**

***We have a limited operating history and have incurred significant losses since our inception and we anticipate that we will continue to incur losses for the foreseeable future.***

We are a clinical-stage biotechnology company, and we have not commercialized any products or generated any revenues from the sale of products. We have incurred losses from operations in each year since our inception, and our net losses were \$8.0 million and \$7.9 million for the years ended December 31, 2012 and 2013, respectively, and \$1.9 million and \$2.8 million for the three months ended March 31, 2013 and 2014, respectively. As of March 31, 2014, we had an accumulated deficit of \$104.8 million. We do not expect to generate any product revenues in the foreseeable future. We do not know whether or when we will generate revenue or become profitable.

We have devoted most of our financial resources to research and development, including our clinical and preclinical development activities. To date, we have financed our operations primarily through the sale of equity securities and convertible debt. Our current product candidate, PRT-201, is in clinical trials and we have no commercial sales, which, together with our limited operating history, make it difficult to assess our future viability. The amount of our future net losses will depend, in part, on the rate of our future expenditures and our ability to obtain funding through equity or debt financings or strategic collaborations. We have not completed pivotal clinical trials for any product candidate and it will be several years, if ever, before we have PRT-201 or any future product candidates ready for commercialization. Even if we obtain regulatory approval to market PRT-201 or any additional product candidates, our future revenues will depend upon the size of any markets in which PRT-201 or any additional product candidates have received approval, our ability to achieve sufficient market acceptance, reimbursement from third-party payors and other factors.

We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. We anticipate that our expenses will increase substantially if and as we:

- continue our clinical development and seek regulatory approval of PRT-201, particularly with respect to its lead indication of radiocephalic AVFs;
- commercialize PRT-201 directly in the United States;
- undertake clinical development of PRT-201 in Europe and establish partnerships for commercialization of PRT-201 in all or parts of Europe;
- pursue additional indications for PRT-201 including clinical development of PRT-201 for brachiocephalic AVFs, patients requiring placement of an AVG and peripheral artery disease, or PAD;
- in-license or acquire additional product opportunities and make milestone or other payments under any in-license agreements;
- establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain marketing approval;
- maintain, protect and expand our intellectual property portfolio;
- attract and retain skilled personnel;

- create additional infrastructure to support our operations as a public company and our product development and planned future; and
- experience any delays or encounter issues with any of the above.

The net losses we incur may fluctuate significantly from quarter to quarter and year to year, such that a period-to-period comparison of our results of operations may not be a good indication of our future performance. In any particular quarter or quarters, our operating results could be below the expectations of securities analysts or investors, which could cause our stock price to decline.

***We will require substantial additional financing to achieve our goals, and a failure to obtain this necessary capital when needed on acceptable terms, or at all, could force us to delay, limit, reduce or terminate our product development, any commercialization efforts or other operations.***

Our operations have consumed substantial amounts of cash since inception. As of March 31, 2014, our cash, cash equivalents and investments were \$3.6 million. Our research and development expenses were \$5.9 million and \$4.0 million for the fiscal years ended December 31, 2012 and December 31, 2013, respectively, and \$1.1 million and \$1.2 million for the three-months ended March 31, 2013 and March 31, 2014, respectively. We believe that we will continue to expend substantial resources for the foreseeable future developing PRT-201 and any additional product candidates. These expenditures will include costs associated with research and development, potentially acquiring new technologies, potentially obtaining regulatory approvals and manufacturing products, as well as marketing and selling products approved for sale, if any. In addition, other unanticipated costs may arise. Because the outcome of our planned and anticipated clinical trials is highly uncertain, we cannot reasonably estimate the actual amounts necessary to successfully complete the development and commercialization of PRT-201 or any additional product candidates.

We are currently planning to begin enrolling patients in our first Phase 3 clinical trial of PRT-201 during the third quarter of 2014 for patients undergoing placement of radiocephalic AVFs. Prior to completing enrollment in our first Phase 3 trial, we expect to initiate the second Phase 3 trial. Based on our current operating plan, and absent any future financings or strategic partnerships, we believe that the net proceeds we receive from this offering, and our existing cash and cash equivalents and investments will be sufficient to fund our projected operating expenses and capital expenditure requirements through \_\_\_\_\_, allowing us to obtain results from our first Phase 3 clinical trial of PRT-201 in radiocephalic AVFs. This period could be shortened if there are any significant increases beyond our expectations in spending on development programs or more rapid progress of development programs than anticipated. We do not expect our existing capital resources, including the net proceeds from this offering, to be sufficient to enable us to complete our second Phase 3 trial. Moreover, we do not expect to be able to initiate any other trials, including those for other indications of PRT-201, prior to receiving and reviewing data from our first Phase 3 clinical trial. Furthermore, our operating plan may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned, through public or private equity or debt financings, government or other third-party funding, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements, or a combination of these approaches. Even if we believe we have sufficient funds for our current or future operating plans, we may seek additional capital if market conditions are favorable or if we have specific strategic considerations.

Any additional fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize PRT-201 or any additional product candidates. In addition, we cannot guarantee that future financing will be available in sufficient amounts or on terms acceptable to us, or at all. We could also be required to seek funds through arrangements with collaborative partners or otherwise at an earlier stage than would otherwise be ideal and we may be required to relinquish rights to PRT-201 or any additional product candidates, or otherwise agree to terms

unfavorable to us, any of which may have a material adverse effect on our business, operating results and prospects.

If we are unable to obtain funding on a timely basis, we may be required to significantly curtail, delay or discontinue one or more of our research or development programs or the commercialization of any approved products or be unable to expand our operations or otherwise capitalize on our business opportunities, as desired, which could materially adversely affect our business, financial condition and results of operations.

***We have never generated any revenue from product sales and may never be profitable.***

As a company, we have never obtained regulatory approval for, or commercialized, any product candidate. Our ability to generate substantial revenue and achieve profitability depends on our ability, alone or with strategic collaboration partners, to successfully complete the development of, and obtain the regulatory approvals necessary to commercialize PRT-201 or any additional product candidates. We do not anticipate generating revenues from product sales for at least the next several years, if ever. If PRT-201 or any additional product candidates fail in clinical trials or do not gain regulatory approval, or if PRT-201 or any additional product candidates, if approved, fail to achieve market acceptance, we may never become profitable. Even if we achieve profitability in the future, we may not be able to sustain profitability in subsequent periods. Our ability to generate future revenues from product sales depends heavily on our success in:

- completing clinical development of PRT-201 for one or more indications and research and preclinical and clinical development of any additional product candidates;
- seeking and obtaining regulatory and marketing approvals for PRT-201 if and when we complete clinical trials;
- establishing and maintaining supply and manufacturing relationships with third parties that can provide adequate (in amount and quality) products and services to support clinical development and the market demand for PRT-201, if approved;
- launching and commercializing PRT-201 if we obtain regulatory and marketing approval, either by collaborating with a partner or, if launched independently, by establishing a sales, marketing and distribution infrastructure;
- obtaining and maintaining adequate coverage and reimbursement from third-party payors for PRT-201;
- obtaining market acceptance of PRT-201 as a viable treatment option;
- addressing any competing technological and market developments;
- implementing additional internal systems and infrastructure, as needed;
- identifying and validating new product candidates;
- negotiating favorable terms in any collaboration, licensing or other arrangements into which we may enter;
- maintaining, protecting and expanding our portfolio of intellectual property rights, including patents and know-how;
- developing PRT-201 such that, if approved, it can be commercialized without infringing the intellectual property rights of third parties; and
- attracting, hiring and retaining qualified personnel.

Even if PRT-201 or any additional product candidates that we may develop is approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate. Our expenses could increase beyond expectations if we are required by the FDA, the European Medicines Agency, or EMA, or other regulatory agencies, domestic or foreign, to perform clinical trials and other studies in addition to those that we currently anticipate. Even if we are able to generate revenues from the sale of any approved products, we may not become profitable and may need to obtain additional funding to continue operations. Our failure to become and remain profitable would

depress the market price of our common stock and could impair our ability to raise capital, expand our business, diversify our product offerings or continue our operations. A decline in the value of our company could also cause you to lose all or part of your investment.

### **Risks Related to Clinical Development, Regulatory Review and Approval of Our Product**

***We are substantially dependent on the success of our current product candidate, PRT-201, and cannot guarantee that this product candidate will successfully complete Phase 3 clinical trials, receive regulatory approval or be successfully commercialized.***

We currently have no products approved for commercial distribution. We have invested substantially all of our efforts and financial resources in the development of our current product candidate, PRT-201. Our business depends entirely on the successful development and commercialization of PRT-201, in vascular access or additional indications, which may never occur. Our ability to generate revenues in the near term is substantially dependent on our ability to develop, obtain regulatory approval for, and then successfully commercialize PRT-201. We currently generate no revenues from sales of any products, and we may never be able to develop or commercialize a marketable product.

PRT-201 will require additional clinical development, regulatory approval, commercial manufacturing arrangements, establishment of a commercial organization, significant marketing efforts and further investment before we generate any revenues from product sales. We are not permitted to market or promote PRT-201 for any indication before we receive regulatory approval from the FDA or comparable foreign regulatory authorities, and we may never receive such regulatory approval for any of our product candidates. If we do not receive FDA approval for, and successfully commercialize, PRT-201, we will not be able to generate revenue from PRT-201 in the United States in the foreseeable future, or at all. Any significant delays in obtaining approval for and commercializing PRT-201 will have a substantial adverse impact on our business and financial condition.

We have not previously submitted a BLA to the FDA, or similar drug approval filings to comparable foreign authorities, for any product candidate, and we cannot be certain that PRT-201 or any additional product candidates will be successful in clinical trials or receive regulatory approval. In our Phase 2 clinical trial, our primary efficacy endpoint of primary unassisted patency did not show statistically significant benefit for the 30 microgram dose versus placebo with regard to primary unassisted patency. While statistical analyses of the subset of patients with radiocephalic AVFs suggested a clinically significant benefit over placebo for that patient subset, those analyses were not prespecified, and we cannot assure you that these results will be repeated in our Phase 3 trials. Following completion of the trial we analyzed the data in a number of ways in addition to the analysis specified in the protocol for the Phase 2 clinical trial of PRT-201. For example, we analyzed the data from the subset of patients undergoing placement of a radiocephalic AVF. Analysis of data in a manner or from subsets that were not prespecified in the protocol is typically not sufficient to serve as the basis for regulatory approval and is generally not considered as reliable as analyses which were prespecified in the protocol. Even though our Phase 3 trials will enroll patients undergoing a surgical procedure to create a radiocephalic AVF (i.e., that subset of patients in which PRT-201 showed a greater benefit in our Phase 2 clinical trial), there are risks of failure inherent at any stage of product development, and we may not demonstrate efficacy with regard to the primary endpoint of our planned Phase 3 clinical trials, or unexpected adverse events may appear. Further, PRT-201 or any additional product candidates, may not receive regulatory approval even if they are successful in clinical trials. If approved for marketing by applicable regulatory authorities, our ability to generate revenues from PRT-201 will depend on our ability to:

- create market demand for PRT-201 through our own marketing and sales organization, and any other arrangements to promote this product candidate we may otherwise establish;
- hire, train and deploy a specialty hospital sales force, focused primarily on vascular surgeons, to commercialize PRT-201 in the United States;

- manufacture PRT-201 in sufficient quantities and at acceptable quality and manufacturing cost to meet commercial demand at launch and thereafter and establish and maintain agreements with wholesalers, distributors and group purchasing organizations on commercially reasonable terms;
- create partnerships with third parties to promote and sell PRT-201 in any foreign markets where we receive marketing approval;
- maintain patent protection and regulatory exclusivity for PRT-201;
- launch commercial sales of PRT-201, whether alone or in collaboration with others;
- achieve appropriate reimbursement for PRT-201;
- effectively compete with other products; and
- maintain a continued acceptable safety profile of PRT-201 following launch.

As we continue to develop PRT-201 for other indications, including AVG, brachiocephalic AVF and PAD, or additional product candidates, we will face similar risks and challenges.

***Clinical development is a lengthy and expensive process with an uncertain outcome due to many factors. Because the results of early clinical trials are not necessarily predictive of future results, PRT-201 may not have favorable results in later clinical trials or receive regulatory approval.***

Clinical development is expensive, difficult to design and implement, takes many years to complete and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process and PRT-201 is subject to the risks of failure inherent in drug and biological development, including failure to demonstrate efficacy in a pivotal clinical trial or in the patient population we intend to enroll, the occurrence of severe or medically or commercially unacceptable adverse events, failure to comply with protocols or applicable regulatory requirements and determination by the FDA or any comparable foreign regulatory authority that a drug and biological product is not approvable. Trends and results observed in earlier stage clinical trials, particularly trends and results observed through analysis of the data which was not prespecified in the protocol, may not be replicated in later stage clinical trials. For example, as is common with Phase 2 trials, we explored a number of endpoints and analyzed the data from our Phase 2 clinical trial of PRT-201 in a number of ways, some of which were not prespecified. Product candidates such as PRT-201 in Phase 3 clinical trials may fail to demonstrate sufficient efficacy despite having progressed through initial clinical trials, even if certain non-prespecified analyses of primary or secondary endpoints in those early trials showed trends toward efficacy or, in some analyses, statistical significance. Companies frequently suffer significant setbacks in late-stage clinical trials due to lack of efficacy, manufacturing or formulation changes or adverse safety profiles, even after earlier clinical trials have shown promising results. During the course of our clinical development, we modified our PRT-201 finished product formulation for our Phase 3 trials and commercial launch in order to facilitate ease of administration and fill and finish of vials at our 30 microgram dose. Our formulation changes could adversely affect results in our clinical trials, requiring us to make further formulation changes. Additional changes could cause us to delay or repeat clinical trials, and we could incur unexpected costs that would have an adverse effect on our business, operating results and prospects.

The design of a clinical trial can determine whether its results will support approval of a product, and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced or completed. Proteon has limited experience in designing clinical trials and may be unable to design and execute a clinical trial to support marketing approval. In addition, preclinical and clinical data are often susceptible to varying interpretations and analyses. Many companies that believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval for the product candidates. Even if we believe that the results of clinical trials for our product candidates warrant marketing approval, the FDA or comparable non-United States regulatory authorities may disagree and may not grant marketing approval of PRT-201 or any additional product candidates.

In some instances, there can be significant variability in safety or efficacy results between different clinical trials of the same product candidate due to numerous factors, including changes in trial procedures

set forth in protocols, differences in the size and type of the patient populations, changes in and adherence to the clinical trial protocols and the rate of dropout among clinical trial participants. Any Phase 3 or other clinical trial that we may conduct may not demonstrate the efficacy and safety necessary to obtain regulatory approval to market PRT-201 or any additional product candidate.

Any delay or failure in our clinical trials would delay our obtaining, or make us unable to obtain, applicable regulatory approvals, which would prevent us from commercializing PRT-201 or any additional product candidates, generating revenues and achieving and sustaining profitability.

***If clinical trials of PRT-201 or any additional product candidates fail to demonstrate safety and efficacy to the satisfaction of the FDA and comparable non-United States regulators, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of PRT-201 or any additional product candidates.***

We are not permitted to commercialize, market, promote or sell any product candidate in the United States without obtaining marketing approval from the FDA. Comparable non-United States regulatory authorities, such as the EMA, impose similar restrictions. We may never receive such approvals. We must have completed extensive preclinical development and clinical trials to demonstrate the safety and efficacy of the product candidate in humans before we will be able to obtain these approvals. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is inherently uncertain as to outcome.

Any inability to successfully complete clinical development could result in additional costs to us and impair our ability to generate revenues from product sales, regulatory and commercialization milestones and royalties. In addition, if (1) we are required to conduct additional clinical trials or other testing of PRT-201 beyond the trials and testing that we contemplate, (2) we are unable to successfully complete clinical trials of PRT-201 or any additional product candidates or other testing, (3) the results of these trials or tests are unfavorable, uncertain or are only modestly favorable or (4) there are unacceptable safety concerns associated with PRT-201 or any additional product candidates, we, in addition to incurring additional costs, may:

- be delayed in obtaining marketing approval for PRT-201 or any additional product candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as we intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or significant safety warnings, including boxed warnings;
- be subject to additional post-marketing testing or other requirements; or
- be required to remove the product from the market after obtaining marketing approval.

In general, the FDA requires two adequate and well-controlled clinical trials to demonstrate the effectiveness of a product candidate. If the results of our first Phase 3 clinical trial are sufficiently compelling, we intend to meet with the FDA to discuss the possibility of submitting a BLA supported by the single Phase 3 trial and may decide to submit a BLA to the FDA prior to completing the second Phase 3 trial. If we attempt to rely on a single Phase 3 trial to demonstrate the effectiveness of PRT-201, the usual demonstration of the statistical significance in the primary efficacy endpoint ( $p=0.05$ ) is unlikely to be sufficient to obtain approval of PRT-201, and we would likely be required to demonstrate more robust statistical significance. Even with a robust  $p$ -value, the FDA may not consider the results of the single Phase 3 trial to be sufficient for BLA filing or approval, and may require that we conduct additional trials.

***We may be unable to obtain regulatory approval for PRT-201 or any additional product candidates under applicable regulatory requirements. The denial or delay of any approvals would prevent or delay commercialization and have a material adverse effect on our potential to generate revenue, our business and our results of operations.***

PRT-201 and any additional product candidates are subject to extensive governmental regulations relating to, among other things, research, clinical trials, approval, manufacturing, recordkeeping, labeling, storage, advertising, promotion, distribution, import, export and commercialization. In order to obtain regulatory approval for the commercial sale of any product candidate, we must demonstrate through extensive preclinical studies and clinical trials that the product candidate is safe and effective for use in each target indication. Failure to obtain marketing approval for a product candidate will prevent us from commercializing the product candidate. PRT-201 is still in development and is subject to the risks of failure inherent in drug or biologic development. We have not received approval to market any product candidate from regulatory authorities in any jurisdiction. Proteon has only limited experience in conducting and managing the clinical trials, and in submitting and supporting the applications necessary to gain marketing approvals and expect to rely on third-party clinical research organizations to assist us in this process. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities. PRT-201 may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use. We may gain regulatory approval for PRT-201 or any additional product candidates in some but not all of the territories available or some but not all of the target indications, resulting in limited commercial opportunity for the product, or we may never obtain regulatory approval for PRT-201 or any additional product candidates in any jurisdiction.

The process of obtaining marketing approvals, both in the United States and abroad, is expensive, may take many years if additional clinical trials are required, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. The FDA and foreign regulatory authorities also have substantial discretion in the drug and biologics approval process. The number and types of preclinical studies and clinical trials that will be required for regulatory approval varies depending on the product candidate, the disease or condition that the product candidate is designed to address, and the regulations applicable to any particular product candidate. Approval policies, regulations or the type and amount of clinical data necessary to gain approval may change during the course of a product candidate's clinical development and may vary among jurisdictions, and there may be varying interpretations of data obtained from preclinical studies or clinical trials, either of which may cause delays or limitations in the approval or the decision not to approve an application. Regulatory agencies can delay, limit or deny approval of a product candidate for many reasons, including:

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a product candidate is safe and effective for its proposed indications;
- the results of later-stage clinical trials may not meet the level of statistical or clinical significance required by the FDA or comparable foreign regulatory authorities for approval;
- the results of later-stage clinical trials may not confirm the positive results from earlier preclinical studies or clinical trials;
- we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data from preclinical studies or clinical trials;

- the data collected from clinical trials of PRT-201 or any additional product candidate may not be sufficient to the satisfaction of the FDA or comparable foreign regulatory authorities to support the submission of a BLA, or other comparable submission in foreign jurisdictions or to obtain regulatory approval in the United States or elsewhere;
- our manufacturing processes or facilities may not be adequate to support approval of our product candidates; or
- regulatory agencies may change their approval policies or adopt new regulations in a manner rendering our clinical data insufficient for approval.

It is possible that neither PRT-201 nor any product candidates we may seek to develop in the future will ever obtain the appropriate regulatory approvals necessary for us or any future collaborators to commence product sales. Any delay in obtaining, or failure to obtain, required approvals would materially adversely affect our ability to generate revenue from the particular product candidate, which likely would result in significant harm to our financial position and adversely impact our stock price.

***We may face difficulty in enrolling patients for clinical trials.***

We may find it difficult to enroll patients in our clinical trials, which could delay or prevent clinical trials of PRT-201 or any additional product candidates. We have never previously limited a trial to patients undergoing a surgical procedure to create a radiocephalic AVF, as we will do for our Phase 3 trials. Identifying and qualifying patients to participate in clinical trials of PRT-201 or any additional product candidates are critical to our success. The timing of our clinical trials depends on the speed at which we can recruit patients to participate in testing product candidates. The enrollment timeline for radiocephalic AVF patients is lengthy and there are limited numbers of sites from which we can enroll pre-hemodialysis or hemodialysis patients. If patients are unwilling to participate in our trials because of negative publicity from adverse events or for other reasons, including competitive clinical trials for similar patient populations, the timeline for recruiting patients, conducting trials and obtaining regulatory approval of potential products may be delayed or prevented. These delays could result in increased costs, delays in advancing our product development, delays in testing the effectiveness of our technology or termination of the clinical trials altogether. We may not be able to identify, recruit and enroll a sufficient number of patients, or those with required or desired characteristics to achieve diversity in a trial, to complete our clinical trials in a timely manner. Patient enrollment is affected by factors including:

- severity of the disease under investigation;
- design of the trial protocol;
- size of the patient population;
- eligibility criteria for the trial in question;
- perceived risks and benefits of the product candidate under study;
- proximity and availability of clinical trial sites for prospective patients;
- availability of competing therapies and clinical trials;
- efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians; and
- ability to monitor patients adequately during and after treatment.

We may not be able to initiate or continue clinical trials if we cannot enroll a sufficient number of eligible patients to participate in the clinical trials required by regulatory agencies. If we have difficulty enrolling a sufficient number of patients to conduct our clinical trials as planned, we may need to delay, limit or terminate ongoing or planned clinical trials, any of which would have an adverse effect on our business.



***If we experience any of a number of possible unforeseen events in connection with clinical trials of PRT-201 or any additional product candidates, potential marketing approval or commercialization of PRT-201 or any additional product candidates could be delayed or prevented.***

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent marketing approval of PRT-201 or any additional product candidates, including:

- trials of PRT-201 or any additional product candidates may produce unfavorable or inconclusive results;
- we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- our third party contractors, including those manufacturing PRT-201 or any additional product candidates or components for commercial use or ingredients thereof or conducting clinical trials on our behalf, may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner or at all;
- regulators or institutional review boards may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may have to suspend or terminate clinical trials of PRT-201 or any additional product candidates for various reasons, including a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics of a product candidate;
- regulators or institutional review boards may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or their respective standards of conduct, a finding that the participants are being exposed to unacceptable health risks, undesirable side effects or other unexpected characteristics of the product candidate or findings of undesirable effects caused by a chemically or mechanistically similar biologic or biologic candidate;
- we may experience delays in reaching or fail to reach agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- patient enrollment in these clinical trials may be slower than we anticipate and is limited to a select number of sites, which could cause significant delays given the prolonged enrollment period;
- participants may drop out of these clinical trials at a higher rate than we anticipate and we may not be able to obtain the follow up data for the 12 month period planned in our Phase 3 trial;
- patients who enroll in a clinical trial may misrepresent their eligibility to do so or may otherwise not comply with the clinical trial protocol, resulting in the need to drop the patients from the clinical trial, increase the needed enrollment size for the clinical trial beyond the 300 proposed for each Phase 3 trial or may extend the clinical trial's duration;
- the FDA or comparable foreign regulatory authorities may disagree with our clinical trial design or our interpretation of data from preclinical studies and clinical trials;
- the FDA or comparable foreign regulatory authorities may fail to approve or subsequently find fault with the manufacturing processes or facilities of third party manufacturers with which we enter into agreements for clinical and commercial supplies;
- our finished product that has been manufactured for the PRT-201 Phase 3 trials may be inadequate, or the materials or manufactured product candidates necessary to conduct future clinical trials of PRT-201 or any additional product candidates may be insufficient, inadequate or not available at an acceptable cost, or we may experience interruptions in supply; and
- the approval policies or regulations of the FDA or comparable foreign regulatory authorities may significantly change in a manner rendering our clinical data insufficient to obtain marketing approval.

Product development costs for us will increase if we experience delays in testing or pursuing marketing approvals and we may be required to obtain additional funds to complete clinical trials and prepare for possible commercialization of PRT-201 or any additional product candidates. We do not know whether any

clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize PRT-201 or any additional product candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize PRT-201 or any additional product candidates and may harm our business and results of operations. In addition, many of the factors that cause, or lead to, clinical trial delays may ultimately lead to the denial of marketing approval of PRT-201 or any additional product candidates.

***Any product for which we obtain FDA approval will be subject to extensive ongoing regulatory requirements, and Proteon may be subject to penalties if it fails to comply with regulatory requirements or if it experiences unanticipated problems with its products, when and if any of them are approved.***

Any product for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical research, labeling, advertising and promotional activities for such product, will be subject to continual requirements of and review by, the FDA and comparable regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, current good manufacturing practices, or cGMP requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. We must also comply with requirements concerning advertising and promotion for PRT-201 or any additional product candidates for which we obtain marketing approval. Promotional communications with respect to prescription drugs, including biologics, are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved labeling. Thus, we will not be able to promote any products we develop for indications or uses for which they are not approved.

Even if regulatory approval of a product is granted, the approval will be subject to limitations on the indicated uses for which the product may be marketed and may be subject to other conditions of approval. We and our contract manufacturers could be subject to periodic unannounced inspections by the FDA to monitor and ensure compliance with cGMPs. In addition, approval may contain requirements for costly post-marketing testing and surveillance to monitor the safety or efficacy of the product. Discovery after approval of previously unknown problems with any such products, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in actions such as:

- restrictions on our ability to conduct clinical trials, including full or partial clinical holds on ongoing or planned trials;
- restrictions on such products' manufacturing processes;
- restrictions on the marketing of a product;
- restrictions on product distribution;
- requirements to conduct post-marketing clinical trials;
- untitled or Warning Letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- fines, restitution or disgorgement of profits or revenue;
- suspension or withdrawal of regulatory approvals;
- refusal to permit the import or export of our products;
- product seizure;
- injunctions; or
- imposition of civil or criminal penalties.

Accordingly, assuming we receive marketing approval for PRT-201 or any additional product candidates, we and our contract manufacturers will continue to expend time, money and effort in all areas

of regulatory compliance, including manufacturing, production, product surveillance, post-marketing studies and quality control.

***PRT-201 may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial profile of approved labeling, or result in significant negative consequences following any potential marketing approval.***

As with many pharmaceutical and biological products, treatment with PRT-201 or any additional product candidates may produce undesirable side effects or adverse reactions or events. These adverse events may occur despite our belief, based on our preclinical and clinical trials to date, that our PRT-201 has a safety profile that will support approval if we successfully complete of our planned Phase 3 clinical program.

Based on our Phase 2 trial, adverse side effects that could occur with treatment with PRT-201 include AVF surgical incision pain, venous stenosis, AVF thrombosis, steal syndrome and hypoesthesia. If any of these adverse events occur in rates or severity exceeding placebo and unacceptable to regulatory authorities, or unknown serious events emerge, our clinical trials could be suspended or terminated and the FDA, the EMA or other foreign regulatory authorities could order us to cease further development of, or deny approval of, PRT-201 or any additional product candidates for any or all targeted indications, or they could require limitations or onerous warnings on the product label. The product-related side effects could affect patient recruitment or the ability of enrolled patients to complete the trial. If we elect or are required to delay, suspend or terminate any clinical trial of PRT-201 or any additional product candidates, the commercial prospects of such product candidates will be harmed and our ability to generate product revenues from any of these product candidates will be delayed or eliminated. Any of these occurrences may harm our business, financial condition and prospects significantly.

***We may not be able to maintain orphan drug designation or obtain or maintain orphan drug exclusivity for PRT-201***

We have obtained orphan drug designation from the FDA for PRT-201. In the United States, under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals in the United States.

Orphan drug exclusivity may be lost if the FDA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the product to meet the needs of patients with the rare disease or condition.

Even if we obtain orphan drug exclusivity for PRT-201, that exclusivity may not effectively protect the product from competition because different products can be approved for the same condition. Even after an orphan product is approved, the FDA can subsequently approve the same product for the same condition if the FDA concludes that the later product is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care.

***We may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.***

Because we have limited financial and managerial resources, we have focused on developing one product candidate, PRT-201, and have focused on developing this product candidate for specific indications that we identify as most likely to succeed, in terms of both its regulatory approval and commercialization. As such, we are currently primarily focused on the development of PRT-201 for vascular access, and our Phase 3 trials will be limited to the application of PRT-201 in radiocephalic AVFs. In the future we intend to pursue additional indications such as the application of PRT-201 in brachiocephalic AVF placement and/or patients undergoing placement of an AVG. As a result, we may

forego or delay pursuit of opportunities with other product candidates or for other indications that may prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

***Even if we obtain and maintain approval for PRT-201 or additional product candidates from the FDA, we may never obtain approval for PRT-201 or additional product candidates outside of the United States, which would limit our market opportunities and adversely affect our business.***

Even if we obtain approval of a product candidate in the United States by the FDA, such approval does not ensure approval of such product candidate by regulatory authorities in other countries or jurisdictions, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other foreign countries or by the FDA. Sales of PRT-201 or any additional product candidates outside of the United States will be subject to foreign regulatory requirements governing clinical trials and marketing approval. Even if the FDA grants marketing approval for a product candidate, comparable regulatory authorities of foreign countries must also approve the manufacturing and marketing of the product candidate in those countries. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from, and greater than, those in the United States, including additional preclinical studies or clinical trials. In many countries outside the United States, a product candidate must be approved for reimbursement before it can be approved for sale in that country. In some cases, the price that we intend to charge for our products, if approved, is also subject to approval.

Based on additional data including the data from our Phase 3 clinical trials and assuming sufficient funds become available, we plan to commence a clinical trial of PRT-201 in Europe for patients undergoing placement of radiocephalic AVFs. Prior to enrolling our first patient in Europe, we plan to formally seek guidance from the EMA regarding its requirements for regulatory approval. We expect results from this trial to be available two to three years after the first patient is enrolled. If results of this European trial successfully meet its primary endpoint and depending on the guidance obtained from the EMA, we would expect to submit a Marketing Authorization Application, or MAA, following our receipt of the trial results. Obtaining an approval is a lengthy and expensive process and the EMA has its own procedures for approval of product candidates. Even if a product candidate is approved, the EMA may limit the indications for which the product may be marketed, require extensive warnings on the product labeling or require expensive and time-consuming clinical trials or reporting as conditions of approval. Regulatory authorities in countries outside of the United States and Europe also have requirements for approval of product candidates with which we must comply prior to marketing in those countries. Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of PRT-201 or any additional product candidates in certain countries.

***If we are found in violation of federal or state "fraud and abuse" laws or other healthcare laws and regulations, we may be required to pay a penalty and/or be suspended from participation in federal or state healthcare programs, which may adversely affect our business, financial condition and results of operation.***

We may also be subject to various federal and state laws pertaining to healthcare "fraud and abuse," including anti-kickback laws and false claims laws. Anti-kickback laws make it illegal for a prescription drug or biologic manufacturer to solicit, offer, receive or pay any remuneration in exchange for, or to induce, the referral of business, including the purchase or prescription of a particular drug or biologic. Due

to the breadth of the statutory provisions, it is possible that our practices might be challenged under anti-kickback or other fraud and abuse laws. Moreover, recent healthcare reform legislation has strengthened these laws. For example, the recently enacted Patient Protection and Affordable Care Act, or ACA, among other things, amends the intent requirement of the federal anti-kickback and criminal healthcare fraud statutes to clarify that a person or entity does not need to have actual knowledge of this statute or specific intent to violate it. In addition, the ACA clarifies that the government may assert that a claim that includes items or services resulting from a violation of the federal anti-kickback statute constitutes a false or fraudulent claim for purposes of the false claims statutes. False claims laws prohibit anyone from knowingly and willingly presenting, or causing to be presented for payment, to government third-party payors (including Medicare and Medicaid) claims for reimbursed drugs, or biologics or services that are false or fraudulent, claims for items or services not provided as claimed, or claims for medically unnecessary items or services. Our activities relating to the sale and marketing of our products may be subject to scrutiny under these laws. Violations of fraud and abuse laws are punishable by criminal and civil sanctions, including fines and civil monetary penalties, the possibility of exclusion from federal healthcare programs (including Medicare and Medicaid) and corporate integrity agreements, which impose, among other things, rigorous operational and monitoring requirements on companies.

Given the significant penalties and fines that can be imposed on companies and individuals if convicted, allegations of violations often result in settlements even if the company or individual being investigated admits no wrongdoing. Settlements often include significant civil sanctions, including fines and civil monetary penalties, and corporate integrity agreements. If the government were to allege or convict us or our executive officers of violating these laws, our business could be harmed. In addition, private individuals have the ability to bring similar actions under the False Claims Act. Our activities could be subject to challenge for the reasons discussed above and due to the broad scope of these laws and the increasing attention being given to them by law enforcement authorities. Further, an increasing number of state laws require manufacturers to make reports to states on pricing and marketing information. Many of these laws contain ambiguities as to what is required to comply with the laws. Given the lack of clarity in laws and their implementation, our reporting actions could be subject to the penalty provisions of the pertinent state authorities.

Similar rigid restrictions are imposed on the promotion and marketing of medicinal products in the European Union and other countries. Laws (including those governing promotion, marketing and anti-kickback provisions), industry regulations and professional codes of conduct often are strictly enforced. Even in those countries where we are not directly responsible for the promotion and marketing of our products, inappropriate activity by our international distribution partners can have adverse implications for us.

***We may not be able to comply with requirements of foreign jurisdictions in conducting trials outside of the United States.***

To date, we have not conducted any clinical trials outside of the United States. Our ability to successfully initiate, enroll and complete a clinical trial in any foreign country, should we attempt to do so, is subject to numerous risks unique to conducting business in foreign countries, including:

- difficulty in establishing or managing relationships with contract research organizations, or CROs, and physicians;
- different standards for the conduct of clinical trials;
- our inability to locate qualified local consultants, physicians and partners;
- the potential burden of complying with a variety of foreign laws, medical standards and regulatory requirements, including the regulation of pharmaceutical and biotechnology products and treatment; and
- the acceptability of data obtained from trials conducted outside the United States to the FDA in support of a BLA.

## Risks Related to Commercialization of Our Product

***If we are unable to establish effective marketing and sales capabilities or enter into agreements with third parties to market and sell our product candidates, if they are approved, we may be unable to generate product revenues.***

We currently do not have a commercial infrastructure for the marketing, sale and distribution of biological products. If approved, in order to commercialize our products, we must build our marketing, sales and distribution capabilities or make arrangements with third parties to perform these services. We may not be successful in doing so. If PRT-201 is approved by the FDA, we plan to build a specialty hospital sales force in the United States of approximately 75-100 representatives, supported by reimbursement specialists and a medical affairs team. We may seek to further penetrate the U.S. market in the future by expanding our sales force or through collaborations with other pharmaceutical or biotechnology companies or third party manufacturing and sales organizations. If approved for marketing outside the United States, we may commercialize outside the United States with our own specialty hospital sales force and/or with a commercial partner.

As a company we have no prior experience in the marketing, sale and distribution of biological products, and there are significant risks involved in the building and managing of a commercial infrastructure. The establishment and development of our own sales force and related compliance plans to market any products we may develop will be expensive and time consuming and could delay any product launch, and we may not be able to successfully develop this capability. We, or our future collaborators, will have to compete with other companies to recruit, hire, train, manage and retain marketing and sales personnel. In the event we are unable to develop a marketing and sales infrastructure, we may not be able to commercialize PRT-201 or any additional product candidates, which would limit our ability to generate product revenues. Our ability to generate product revenues would be impaired by:

- our inability to recruit, train, manage and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to vascular surgeons or persuade adequate numbers of vascular surgeons to use PRT-201 or any additional product candidates;
- our inability to effectively oversee a geographically dispersed sales and marketing team; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

Although our current plan is to hire most of our sales and marketing personnel only if PRT-201 is approved by the FDA, we will incur expenses prior to product launch in recruiting this sales force and developing a marketing and sales infrastructure. If the commercial launch of PRT-201 is delayed as a result of FDA requirements or other reasons, we would incur these expenses prior to being able to realize any revenue from sales of PRT-201. Even if we are able to effectively hire a sales force and develop a marketing and sales infrastructure, our sales force and marketing teams may not be successful in commercializing PRT-201 or any additional product candidates.

In the event we are unable to hire a sales force or collaborate with a third-party marketing and sales organization to commercialize any approved product candidates outside the United States, our ability to generate product revenues may be limited. To the extent we rely on third parties to commercialize any products for which we obtain regulatory approval, we may receive less revenues than if we commercialized these products ourselves. In addition, we would have less control over the sales efforts of any other third parties involved in our commercialization efforts.

***Even if PRT-201 or any additional product candidates receive regulatory approval, they may fail to achieve the broad degree of physician adoption and use necessary for commercial success.***

The commercial success of PRT-201 and any product candidates that we may develop will depend upon the degree of market acceptance by physicians, patients, healthcare payors and others in the medical

community. Even if the FDA approves PRT-201 or one or more of our future product candidates, physicians and patients may not accept and use them. Acceptance and use of any of our products will depend upon a number of factors including:

- perceptions by members of the healthcare community, including physicians, about the safety and effectiveness of our products;
- cost-effectiveness of our products relative to any competing products;
- availability of coverage and reimbursement for our products from government or other healthcare payors; and
- effectiveness of marketing and distribution efforts by us and our licensees and distributors, if any.

Because we expect sales of PRT-201, if approved, to generate substantially all of our product revenues for the foreseeable future, the failure of PRT-201 to gain market acceptance would harm our business and would require us to seek additional financing.

***PRT-201 or any additional product candidates, if approved, may face significant competition and our failure to effectively compete may prevent us from achieving significant market penetration and expansion.***

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. We face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, medical device companies, academic institutions, governmental agencies and public and private research institutions. While we believe that PRT-201's features, safety and efficacy, will differentiate it from any competitive products that may become available in the future, we expect to face potential competition from many different sources, including larger and better-funded pharmaceutical, specialty pharmaceutical and biotechnology companies and medical device companies, as well as from academic institutions and governmental agencies and public and private research institutions that may develop potentially competitive products or technologies.

Some of our competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Smaller or early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

The key competitive factors affecting the success of PRT-201, if approved, are likely to be its efficacy, safety, convenience, price, and the availability of reimbursement from government and other third party payors. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, more convenient or less expensive than any products that we may develop. Our competitors may also obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours.

We are not aware of any therapeutic products approved in the United States or Europe for the prevention of vascular access failure. We are aware of other therapies in development with companies including Shire, Vascular Therapies and Celladon. Other potential competition includes new synthetic grafts, including those that may be developed by companies that currently compete in the graft market, such as W.L. Gore, C.R. Bard and Maquet, as well as tissue engineered grafts, including those in development by Cytograft and Humacyte. PRT-201 could face competition from companies developing technologies to provide a more effective anastomosis, including BioConnect Systems, Caymus Medical, Phraxys, CreatiVasc, and TVA Medical. Finally, PRT-201's commercial success could be affected by the development of technologies to improve the outcomes of interventions to restore patency, including stents, stent grafts and drug eluting balloons.

***PRT-201 or any additional product candidates for which we intend to seek approval as biologic products may face competition sooner than anticipated.***

With the enactment of the Biologics Price Competition and Innovation Act of 2009, or BPCIA, as part of the Affordable Care Act, an abbreviated pathway for the approval of biosimilar and interchangeable biological products was created. The abbreviated regulatory pathway establishes legal authority for the FDA to review and approve biosimilar biologics, including the possible designation of a biosimilar as "interchangeable" based on its similarity to an existing brand product. Under the BPCIA, an application for a biosimilar product cannot be approved by the FDA until 12 years after the original branded product was approved under a BLA. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty. While it is uncertain when such processes intended to implement BPCIA may be fully adopted by the FDA, any such processes could have a material adverse effect on the future commercial prospects for our biological products.

We believe that PRT-201 or any additional product candidates approved as a biological product under a BLA should qualify for the 12-year period of exclusivity. However, there is a risk that the FDA will not consider PRT-201 or any additional product candidates to be reference products for competing products, potentially creating the opportunity for generic competition sooner than anticipated. Additionally, this period of regulatory exclusivity does not apply to companies pursuing regulatory approval via their own traditional BLA, rather than via the abbreviated pathway. Moreover, the extent to which a biosimilar, once approved, will be substituted for any one of our reference products in a way that is similar to traditional generic substitution for non-biological products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing.

***If the government or third-party payors fail to provide coverage and adequate coverage and payment rates for PRT-201 or any additional product candidates or if surgeons or hospitals choose not to use PRT-201, our revenue and prospects for profitability will be limited.***

In both domestic and foreign markets, sales of our future products will depend in part upon the availability of coverage and reimbursement from third-party payors. The majority of incident and prevalent hemodialysis patients have Medicare coverage and other third-party payors include other government health programs such as Medicaid, managed care providers, private health insurers and other organizations. Coverage decisions may depend upon clinical and economic standards that disfavor new drug products when more established or lower cost therapeutic alternatives are already available or subsequently become available. Assuming coverage is approved, the resulting reimbursement payment rates might not be adequate. Accordingly, PRT-201 or any of our other product candidates, if approved, will face competition from other therapies and drugs for limited financial resources. We may need to conduct post-marketing studies in order to demonstrate the cost-effectiveness of any future products to the satisfaction of outpatient clinics, hospitals, other target customers and their third-party payors. Such studies might require us to commit a significant amount of management time and financial and other resources. Our future products might not ultimately be considered cost-effective. Adequate third-party coverage and reimbursement might not be available to enable us to maintain price levels sufficient to realize an appropriate return on investment in product development.

Third party payors, whether foreign or domestic, or governmental or commercial, are developing increasingly sophisticated methods of controlling healthcare costs. In addition, in the United States, no uniform policy of coverage and reimbursement for drug products exists among third-party payors. Therefore, coverage and reimbursement for drug products can differ significantly from payor to payor. Further, we believe that future coverage and reimbursement will likely be subject to increased restrictions both in the United States and in international markets. Third party coverage and reimbursement for our products or product candidates for which we receive regulatory approval may not be available or adequate in either the United States or international markets, which could have a negative effect on our business, results of operations, financial condition and prospects.



## Risks Related to Dependence on Third Parties

***We and our contract manufacturers are subject to significant regulation with respect to manufacturing our product candidates. The manufacturing facilities on which we rely may not continue to meet regulatory requirements and have limited capacity.***

We currently have a relationship with only one supplier, Lonza AG, for the manufacturing of active pharmaceutical ingredient, or API, for PRT-201 for clinical testing purposes, and intend to continue to utilize Lonza as our sole or primary supplier in the future. We have used two companies, Jubilant HollisterStier and DSM Pharmaceuticals, to vial and make our PRT-201 finished product. We also expect to rely upon third parties to produce materials required for the commercial production of PRT-201 or any additional product candidates if we succeed in obtaining the necessary regulatory approvals.

All entities involved in the preparation of drugs or biologics for clinical trials or commercial sale, including our existing contract manufacturers, are subject to extensive regulation. Ingredients of a finished therapeutic biologic product approved for commercial sale or used in late-stage clinical trials must be manufactured in accordance with cGMP and equivalent foreign standards. These regulations govern manufacturing processes and procedures (including record keeping) and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Poor control of production processes can lead to the introduction of adventitious agents or other contaminants, or to inadvertent changes in the properties or stability of product candidate that may not be detectable in final product testing. We or our contract manufacturers must supply all necessary documentation in support of a BLA on a timely basis and must adhere to the FDA's good laboratory practices, or GLPs, and cGMP regulations enforced by the FDA through its facilities inspection program. Any failure by our third-party manufacturers to comply with cGMP or failure to scale-up manufacturing processes, including any failure to deliver sufficient quantities of product candidates in a timely manner for the process validation required in connection with a BLA filing, could lead to a delay in, or failure to obtain, regulatory approval of PRT-201 or any additional product candidates. For example, on November 27, 2013, our third-party supplier of finished biological product, Jubilant HollisterStier, received a Warning Letter from the FDA alleging that the company was not complying with cGMPs. We received a letter from the FDA on February 13, 2014, stating that the Warning Letter does not impact the batch of finished product we intend to use for our Phase 3 clinical trials. However, this third party or other third parties could encounter similar difficulties that could impede our clinical trials or commercialization. Our facilities and quality systems and the facilities and quality systems of some or all of our third-party contractors must also pass a pre-approval inspection for compliance with the applicable regulations as a condition of regulatory approval of PRT-201 or any additional product candidates. In addition, the regulatory authorities may, at any time, audit or inspect a manufacturing facility involved with the preparation of our product candidate or the associated quality systems for compliance with the regulations applicable to the activities being conducted. If these facilities and quality systems do not pass a pre-approval plant inspection from the FDA or a comparable foreign authority, approval of our product candidate by the FDA or the equivalent approvals in other jurisdictions will not be granted until the regulatory authority is satisfied that the facility complies with applicable regulations.

Regulatory authorities also may, at any time following approval of a product for sale, audit our manufacturing facilities or those of our third-party contractors. If any such inspection or audit identifies a failure to comply with applicable regulations or if a violation of our product specifications or applicable regulations occurs independent of such an inspection or audit, we or the relevant regulatory authority may require remedial measures that may be costly and/or time-consuming for us or a third party to implement and that may include the temporary or permanent suspension of a clinical trial or commercial sales or the temporary or permanent closure of a facility. Any such remedial measures imposed upon us or third parties with whom we contract could materially harm our business.

If we or any of our third-party manufacturers fail to maintain regulatory compliance, the FDA can impose regulatory sanctions including, among other things, refusal to approve a pending application for a new drug or biologic product or revocation of a pre-existing approval. If any such event occurs, our business, financial condition and results of operations may be materially harmed.

***We rely on third parties to conduct some or all aspects of our product manufacturing, protocol development, research, and preclinical and clinical testing, and these third parties may not perform satisfactorily.***

We do not currently, and do not expect in the future, to independently conduct all aspects of our product manufacturing, protocol development, research and monitoring and management of our clinical programs. PRT-201 API is produced by our contract manufacturer, Lonza. PRT-201 finished product is produced by our contract fill/finish provider, Jubilant HollisterStier. Release testing and stability for API and finished product is performed by PPD, Inc. We currently rely, and expect to continue to rely, on third parties with respect to these items. While we will have agreements governing their activities, we will have limited influence over their actual day-to-day performance. Nevertheless, we will be responsible for ensuring that the manufacturing is conducted in accordance with regulatory requirements such as cGMPs. Our reliance on the third parties does not relieve us of our regulatory responsibilities.

Any of these third parties may terminate their engagements with us under the terms of our agreements upon notice to us. If we need to enter into alternative arrangements, our product candidate development activities may be delayed. Our reliance on these third parties for research and development activities reduces our day-to-day control over these activities but does not relieve us of our responsibility to ensure compliance with all required legal, regulatory and scientific standards and any applicable trial protocols. For example, for PRT-201 or any additional product candidates that we develop and commercialize on our own, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with its protocol and analyzed in accordance with its statistical analysis plan for the clinical trial.

If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our studies in accordance with regulatory requirements or our protocols, we may be delayed in completing, or unable to complete, the clinical trials required to support future approval of PRT-201 or any additional product candidates.

We rely on our manufacturers to purchase from third-party suppliers the materials necessary to produce our product candidate, PRT-201, for our clinical trials. There are a small number of suppliers for certain raw materials that we use to manufacture PRT-201. These suppliers may not sell these raw materials to our manufacturers at the times we need them or on commercially reasonable terms. We do not have any control over the process or timing of the acquisition of these raw materials by our manufacturers. Moreover, we currently do not have any agreements for the commercial production of these raw materials. Although the API and the finished product for each of our Phase 3 trials has already been manufactured and is held in storage, we will need supply of finished product as part of the process validation and for any stability or other tests in connection with a BLA application and also to conduct additional clinical trials, for example for additional PRT-201 indications. Any significant delay in the supply of the ingredients thereof due to the need to replace a third-party manufacturer could considerably delay completion of our clinical trials, product testing and potential regulatory approval of PRT-201 or any additional product candidate as we believe that replacing Lonza as the manufacturer of our API would take one to two years. If our manufacturers or we are unable to purchase these raw materials after regulatory approval has been obtained for our product candidate, our ability to commercially launch and/or generate revenues from the sale of any approved product would be impaired. Reliance on third-party manufacturers entails exposure to risks to which we would not be subject if we manufactured the product candidate ourselves, including:

- failure to negotiate manufacturing agreements with third parties under commercially reasonable terms;

- reduced day-to-day control over the manufacturing process for our product candidates as a result of using third-party manufacturers for all aspects of manufacturing activities;
- reduced control over the protection of our trade secrets and know-how from misappropriation or inadvertent disclosure;
- termination or nonrenewal of manufacturing agreements with third parties in a manner or at a time that may be costly or damaging to us or result in delays in the development or commercialization of our product candidates; and
- disruptions to the operations of our third-party manufacturers or suppliers caused by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier.

Any of these events could lead to delays in the development of PRT-201 or any additional product candidates, including delays in our clinical trials, or failure to obtain regulatory approval for our product candidates, or it could impact our ability to successfully commercialize PRT-201 or any additional product candidates. Some of these events could be the basis for FDA or other regulatory action, including injunction, recall, seizure or total or partial suspension of production. Any of these events could have a material adverse effect on our business.

***We rely on third parties to conduct, supervise and monitor our clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval for, or commercialize, PRT-201 or any additional product candidates and our business could be substantially harmed.***

We rely on CROs and clinical trial sites to ensure our clinical trials are conducted properly and on time. While we will have agreements governing their activities, we will have limited influence over their actual day-to-day performance. Nevertheless, we will be responsible for ensuring that each of our clinical trials is conducted in accordance with the applicable protocol, and legal, regulatory and scientific standards and recognize that our reliance on the CROs does not relieve us of our regulatory responsibilities.

We and our CROs are required to comply with the FDA's good clinical practices, or GCPs, for conducting, recording and reporting the results of clinical trials to assure that the data and reported results are credible and accurate and that the rights, integrity and confidentiality of clinical trial participants are protected. The FDA and comparable foreign regulatory authorities enforce these GCPs through periodic inspections of trial sponsors, principal investigators and clinical trial sites. If we or our CROs fail to comply with applicable GCPs, the clinical data generated in our future clinical trials may be deemed unreliable and the FDA, the EMA, or other foreign regulatory authorities may require us to perform additional clinical trials before approving any marketing applications. Upon inspection, the FDA may determine that our clinical trials did not comply with GCPs. In addition, our future clinical trials will require a sufficient number of test subjects to evaluate the safety and effectiveness of PRT-201 or any additional product candidates. Accordingly, if our CROs fail to comply with these regulations or fail to recruit a sufficient number of patients, we may be required to repeat such clinical trials, which would delay the regulatory approval process.

Our CROs are not our employees, and we are therefore unable to monitor on a day-to-day basis whether or not they devote sufficient time and resources to our clinical and nonclinical programs. These CROs may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other product development activities that could harm our competitive position. If our CROs do not successfully carry out their contractual duties or obligations, fail to meet expected deadlines, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements, or for any other reasons, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for, or successfully commercialize, PRT-201 or any additional product candidates. If any such event were to occur, our financial results and the commercial prospects for PRT-201 or any additional product candidates would be harmed, our costs could increase, and our ability to generate revenues could be delayed.

If any of our relationships with these third-party CROs terminates, we may not be able to enter into arrangements with alternative CROs or to do so on commercially reasonable terms. Further, switching or adding additional CROs involves additional costs and requires management time and focus. In addition, a transition period may be required when a new CRO commences work. As a result, delays may occur, which could materially impact our ability to meet our desired clinical development timelines. Though we carefully manage our relationships with our CROs, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects.

We also rely on other third parties to store and distribute our products for the clinical trials that we conduct. Any performance failure on the part of our distributors could delay clinical development or marketing approval of PRT-201 or any additional product candidates or commercialization of our product, if approved, producing additional losses and depriving us of potential product revenue.

***We may seek to form partnerships in the future with respect to PRT-201 or any additional product candidates, and we may not realize the benefits of such partnerships.***

We may form partnerships, create joint ventures or collaborations or enter into licensing arrangements with third parties for the development and commercialization of PRT-201 or any additional product candidates. We face significant competition in seeking appropriate strategic partners and the negotiation process is time-consuming and complex. Any delays in entering into new strategic partnership agreements related to our product candidates could delay the development and commercialization of our product candidates and reduce their competitiveness even if they reach the market. Moreover, we may not be successful in our efforts to establish a strategic partnership or other collaborative arrangement for any additional product candidates because the potential partner may consider that our research and development pipeline is insufficiently developed to justify a collaborative effort, or that PRT-201 or any additional product candidates and programs do not have the requisite potential to demonstrate safety and efficacy in the target population. Even if we are successful in establishing such a strategic partnership or collaboration, we cannot be certain that, following such a strategic transaction or license, we will be able to progress the development and commercialization of the applicable product candidates as envisioned, or that we will achieve the revenues that would justify such transaction.

### **Risks Related to Our Intellectual Property**

***If our efforts to protect our intellectual property related to PRT-201 or any additional product candidates are not adequate, we may not be able to compete effectively in our market.***

We rely upon a combination of patents, patent applications, know-how and confidentiality agreements to protect the intellectual property related to our only product candidate, PRT-201, and will use a similar strategy to protect any additional product candidates. The patent position of biotechnology companies is generally uncertain because it involves complex legal and factual considerations. The standards applied by the United States Patent and Trademark Office, or USPTO, and foreign patent offices in granting patents are not always applied uniformly or predictably. For example, there is no uniform worldwide policy regarding patentable subject matter or the scope of claims allowable in biotechnology patents. The patent applications that we own may fail to result in issued patents with claims that cover PRT-201 or any additional product candidates in the United States or in other countries. There is no assurance that all potentially relevant prior art relating to our patents and patent applications has been found, and prior art that is not before the patent examiners, as well as prior art that is before the patent examiners, could be used by a third party to invalidate a patent or could be relied on to prevent a patent from issuing from a pending patent application. Even if patents do successfully issue and even if these patents cover PRT-201 or any additional product candidates, third parties may challenge their validity, enforceability or scope, which may result in our patents being narrowed or invalidated. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately provide exclusivity for PRT-201 or any additional

product candidates, prevent others from designing around our patents with similar products that are outside the scope of our patents, or prevent others from operating in jurisdictions in which we did not pursue patent protection. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business.

If patent applications we hold with respect to PRT-201 or any additional product candidates fail to issue, if their breadth or strength of protection is threatened, or if they fail to provide meaningful exclusivity for PRT-201 or any additional product candidates, it could dissuade companies from collaborating with us. We own 18 issued patents and own 27 pending patent applications, two of which have been allowed, covering aspects of PRT-201 or its use. We cannot offer any assurances about which, if any, of the pending patent applications will issue as patents, the breadth of any such patents or any of our currently issued patents, or whether any issued patents will be challenged by third parties or will be found invalid and unenforceable if challenged. Any successful challenge to these patent applications, or patents that may issue from them, or to currently issued patents owned by us, could deprive us of rights necessary for the successful commercialization of PRT-201 or any other product candidate that we may develop. Since patent applications in the United States and most other countries are confidential for a period of time after filing, and some remain so until issued, we cannot be certain that we were the first to file a patent application relating to any particular aspect of a product candidate. Furthermore, if third parties have filed such patent applications, an interference proceeding in the United States can be initiated by these third parties, or by the USPTO itself, to determine who was the first to invent any of the subject matter covered by the patent claims of our patents and patent applications.

In the United States, for patent applications filed prior to March 16, 2013, assuming the other requirements for patentability are met, the first to invent is entitled to the patent, while outside the United States, the first to file a patent application is entitled to the patent. Our currently pending patent applications are examined under the system in place before March 16, 2013. Third parties are allowed to submit prior art prior to the issuance of a patent by the USPTO, and may become involved in reexamination, *inter partes* review or interference proceedings challenging our patent rights. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, which could adversely affect our competitive position with respect to third parties.

In addition, patents have a limited lifespan. In most countries, the statutory term of a patent is 20 years from the earliest domestic priority date claimed. In the United States, for applications filed after June 7, 1995, the statutory term of a patent is 20 years from earliest non-provisional priority date claimed. Various extensions of patent protection may be available in particular countries; however, in all circumstances, the life of a patent, and the protection it affords, has a limited term. If we encounter delays in obtaining regulatory approvals, the period of time during which we could market a product under patent protection could be reduced. We expect to seek extensions of patent protection where these are available in any countries where we are prosecuting patents. Such possible extensions include those permitted under the Drug Price Competition and Patent Term Restoration Act of 1984 in the United States, which permits up to five years' extension of patent protection. The scope of protection available during an extension of a patent claiming a product is limited to the approved product itself for approved uses, and the scope of protection available during an extension of a patent claiming a method of using a product is limited to the uses claimed in the patent and approved for the product. The actual length of the extension will depend on the amount of patent term lost while the product was in clinical trials and while the BLA was under review by the FDA. However, the applicable authorities, including the FDA and the USPTO in the United States, and any equivalent regulatory authority in other countries, may not agree with our assessment of whether such extensions are available, and may refuse to grant extensions to our patents, or may grant more limited extensions than we request. If this occurs, our competitors may be able to take advantage of our investment in development and clinical trials by referencing our clinical and preclinical data, and then may be able to launch their product earlier than might otherwise be the case.

Any loss of, or failure to obtain, patent protection could have a material adverse impact on our business. We may be unable to prevent competitors from entering the market with a product that is similar to or the same as our products.

***Confidentiality agreements with employees and third parties may not prevent unauthorized disclosure of proprietary information.***

We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our employees, consultants, scientific advisors and contractors. We also seek to preserve the integrity and confidentiality of our data and know-how by maintaining physical security of our premises and physical and electronic security of our information technology systems. Nonetheless, despite these precautions, agreements or security measures may be breached, and we may not have adequate remedies for any breach. In addition, our know-how may otherwise become known or be independently discovered by competitors. To the extent that our consultants, contractors or collaborators use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

Enforcing a claim that a third party illegally obtained and is using any of our know-how is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the United States sometimes are less willing than United States courts to protect know-how. Misappropriation or unauthorized disclosure of our know-how could impair our competitive position and may have a material adverse effect on our business.

***We may become involved in lawsuits to protect or enforce our intellectual property, which could be expensive, time consuming and unsuccessful, and which may lead to a finding that our patents are invalid and/or unenforceable.***

Competitors may infringe our patents or misappropriate or otherwise violate our intellectual property rights. To counter infringement or unauthorized use, litigation may be necessary to enforce or defend our intellectual property rights, to protect our know-how and/or to determine the validity and scope of our own intellectual property rights. Intellectual property litigation can be expensive and time consuming. Many of our current and potential competitors have the ability to dedicate substantially greater resources to litigate intellectual property rights than we can. Accordingly, despite our efforts, we may not be able to prevent third parties from infringing or misappropriating our intellectual property. Litigation could result in substantial costs and diversion of management resources, which could harm our business and financial results. In addition, in an infringement proceeding, a court may decide that our patents are invalid or unenforceable, and may refuse to stop the other party from using the technology at issue, including on the grounds that our patents are invalid or unenforceable or do not cover the technology in question. An adverse result in any litigation proceeding could put one or more of our patents at risk of being invalidated, held unenforceable or interpreted narrowly. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation.

***Third-party claims of intellectual property infringement or misappropriation may prevent or delay our development and commercialization efforts.***

Our commercial success depends in part on our ability to develop, manufacture, market and sell PRT-201 or any additional product candidates, and to use proprietary technologies without infringing the patents and proprietary rights of third parties. There is a substantial amount of litigation and adversarial proceedings, both within and outside the United States, involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, oppositions, reexamination, and *inter partes* review proceedings before the USPTO and corresponding foreign patent offices. Third parties own patent rights both within and outside the U.S. in the fields in which we are developing and may develop PRT-201 or any additional product candidates. As

the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that PRT-201 or any additional product candidates may be subject to claims of infringement of the patent rights of third parties.

Third parties may assert that we are employing their proprietary technology without authorization. There may be third-party patents or patent applications with claims that may cover PRT-201 or any additional product candidates and/or the use, manufacture, sale and/or offer for sale of PRT-201 or any additional product candidates. We are aware of European Patent No. EP 1 012 307 B1 by Roche Diagnostics GmbH, or the '307 patent, which claims, among other things, autocatalytically cleavable zymogenic precursor of a serine protease wherein a naturally occurring non-autocatalytic cleavage site is replaced in the zymogenic precursor by an autocatalytic cleavage site. The '307 patent expires on August 12, 2018. We currently estimate that the soonest that we will market PRT-201 in Europe is the third quarter of 2018 and more likely in 2020.

In some cases, we may have failed to identify relevant third-party patents or patent applications. For example, applications filed before November 29, 2000, and certain applications filed after that date that will not be filed outside the United States remain confidential until patents issue. Except for the preceding exceptions, patent applications in the United States and elsewhere are generally published but, only after a waiting period of approximately 18 months after the earliest filing. Therefore, patent applications covering PRT-201 or future product candidates could have been filed by others without our knowledge. Additionally, pending patent applications which have been published can, subject to certain limitations, be later amended in a manner that could cover PRT-201 or any additional product candidates and/or the use, manufacture, sale and/or offer for sale of PRT-201 or any additional product candidates.

If any third-party patents were held by a court of competent jurisdiction to cover PRT-201 or any additional product candidates and/or their use, manufacture, sale, and/or offer for sale, the holders of any of these patents would be able to block our ability to develop and commercialize the applicable product candidate until the patent expired or unless we obtain a license. Licenses may not be available on acceptable terms, if at all. Even if we were able to obtain a license, the rights may be nonexclusive, which could result in our competitors gaining access to the same intellectual property. Ultimately, we could be prevented from commercializing a product, or be forced to cease some aspect of our business operations, if, as a result of actual or threatened patent infringement claims, we are unable to enter into licenses on acceptable terms.

Some of our early research of recombinant expression of PRT-201, but not the corresponding development work, utilized some technology under license from a third party. The third party may contend that we use the licensed technology for our commercial recombinant expression of PRT-201. Litigation may be necessary to defend against such a claim. Even if we are successful in defending against such a claim, litigation could result in substantial costs and be a distraction to management. If we are not successful in defending against such a claim, in addition to paying monetary damages, we may have to reconfigure the PRT-201 expression system, which would materially adversely affect our commercial development efforts.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to commercialize PRT-201 or any additional product candidates. We may face a claim of misappropriation if a third party believes that we inappropriately obtained and used trade secrets of that third party. If we are found to have misappropriated a third party's trade secrets, we may be prevented from further using such trade secrets, limiting our ability to develop PRT-201 or any additional product candidates, and we may be required to pay damages.

Defending against claims of patent infringement or misappropriation of trade secrets could be costly and time consuming, regardless of the outcome. Thus, even if we were to ultimately prevail, or to settle at an early stage, any litigation could burden us with substantial unanticipated costs. In addition, litigation or threatened litigation could result in significant demands on the time and attention of our management team, distracting them from the pursuit of other company business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, pay royalties, redesign our infringing products or obtain one or more licenses from third parties, which may be impossible or require substantial time and monetary expenditure.

During the course of any patent or other intellectual property litigation, there could be public announcements of the results of hearings, rulings on motions, and other interim proceedings in the litigation. If securities analysts or investors regard these announcements as negative, the perceived value of our products, programs, or intellectual property could be diminished. Accordingly, the market price of our common stock may decline.

***If we are unable to adequately protect our proprietary technology, or obtain and maintain issued patents which are sufficient to protect our current product candidate, PRT-201, or any additional product candidates, others could compete against us more directly, which would have a material adverse impact on our business, results of operations, financial condition and prospects.***

We strive to protect and enhance the proprietary technologies that we believe are important to our business, including seeking patents intended to cover our products and compositions, their methods of use and any other inventions that are important to the development of our business. We also rely on know-how to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

Our success will depend significantly on our ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to our business, defend and enforce our current patents and any future patents that may issue, preserve the confidentiality of our know-how and operate without infringing the valid and enforceable patents and proprietary rights of third parties. We also rely on know-how and in-licensing opportunities to develop, strengthen and maintain the proprietary position of PRT-201 or any additional product candidates.

We cannot provide any assurances that any of our pending patent applications will mature into issued patents and, if they do, that such patents or our currently issued patents will include claims with a scope sufficient to protect PRT-201 or any additional product candidates or otherwise provide any competitive advantage. For example, one of our patents that may provide coverage for PRT-201 only covers particular formulations. As a result, this patent would not prevent third-party competitors from creating, making and marketing alternative formulations that fall outside the scope of our patent claims. There can be no assurance that any such alternative formulations will not be equally effective.

Moreover, other parties have developed technologies that may be related or competitive to our approach, and may have filed or may file patent applications and may have received or may receive patents that may overlap or conflict with our patent applications, either by claiming the same methods or formulations or by claiming subject matter that could dominate our patent position. Such third party patent positions may limit or even eliminate our ability to obtain patent protection for certain inventions.

The patent positions of biotechnology and pharmaceutical companies, including our patent position, involve complex legal and factual questions, and, therefore, the issuance, scope, validity and enforceability of any patent claims that we may obtain cannot be predicted with certainty. Patents, if issued, may be challenged, deemed unenforceable, invalidated, or circumvented. United States patents and patent applications may also be subject to interference proceedings, *ex parte* reexamination, or *inter partes* review proceedings, and challenges in district court. Patents may be subjected to opposition, revocation proceedings, or comparable proceedings lodged in various foreign, both national and regional, patent



offices. These proceedings could result in either loss of the patent or denial of the patent application or loss or reduction in the scope of one or more of the claims of the patent or patent application. In addition, such proceedings may be costly. Thus, any patents that we may own or exclusively license may not provide any protection against competitors. Furthermore, an adverse decision in an interference proceeding can result in a third party receiving the patent right sought by us, which in turn could affect our ability to develop, market or otherwise commercialize PRT-201 or any additional product candidates.

Furthermore, though a patent is presumed valid and enforceable, its issuance is not conclusive as to its validity or its enforceability and it may not provide us with adequate proprietary protection or competitive advantages against competitors with similar products. Even if a patent issues and is held to be valid and enforceable, competitors may be able to design around our patents, such as using pre-existing or newly developed technology. Other parties may develop and obtain patent protection for more effective technologies, designs or methods. We may not be able to prevent the unauthorized disclosure or use of our technical knowledge or know-how by consultants, vendors, former employees and current employees. The laws of some foreign countries do not protect our proprietary rights to the same extent as the laws of the United States, and we may encounter significant problems in protecting our proprietary rights in these countries. If these developments were to occur, they could have a material adverse effect on our sales.

In addition, proceedings to enforce or defend our patents, if and when issued, could put our patents at risk of being invalidated, held unenforceable, or interpreted narrowly. Such proceedings could also provoke third parties to assert claims against us, including that some or all of the claims in one or more of our patents are invalid or otherwise unenforceable. If any of our patents, if and when issued, covering PRT-201, or any additional product candidates, are invalidated or found unenforceable, our financial position and results of operations would be materially and adversely impacted. In addition, if a court found that valid, enforceable patents held by third parties covered PRT-201, or any additional product candidates, our financial position and results of operations would also be materially and adversely impacted.

The degree of future protection for our proprietary rights is uncertain, and we cannot ensure that:

- any of our patents or pending patent applications, if issued, will include claims having a scope sufficient to protect PRT-201 or any additional product candidates;
- any of our pending patent applications will issue as patents at all;
- we will be able to successfully commercialize product candidates, if approved, before our relevant patents expire;
- we were the first to make the inventions covered by each of our patents and pending patent applications;
- we were the first to file patent applications for these inventions;
- others will not develop similar or alternative technologies that do not infringe our patents;
- others will not use pre-existing technology to effectively compete against us;
- any of our patents will be found ultimately to be valid and enforceable;
- any patents issued to us will provide a basis for an exclusive market for our commercially viable products, will provide us with any competitive advantages or will not be challenged by third parties;
- we will develop additional proprietary technologies or product candidates that are separately patentable; or
- that our commercial activities or products will not infringe the patents or proprietary rights of others.

We rely upon unpatented know-how to maintain our competitive position, which we seek to protect, in part, by confidentiality agreements with our employees and our collaborators and consultants. It is possible that technology relevant to our business will be independently developed by a person that is not a party to such an agreement. Furthermore, if the employees and consultants who are parties to these agreements breach or violate the terms of these agreements, we may not have adequate remedies for any such breach or violation, and our confidential know-how could become known to others through such breaches or

violations. Further, our know-how could otherwise become known or be independently discovered by our competitors. Further, the term of confidentiality requirements for current and terminated agreements with some of our consultants, contract manufacturing or research organizations and other third parties is finite.

***We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property.***

We enter into confidentiality and intellectual property assignment agreements with our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors. These agreements generally provide that inventions conceived by the party in the course of rendering services to us will be our exclusive property. However, these agreements may not be honored and may not effectively assign intellectual property rights to us. For example, even if we have a consulting agreement in place with an academic advisor pursuant to which such academic advisor is required to assign any inventions developed in connection with providing services to us, such academic advisor may not have the right to assign such inventions to us, as it may conflict with his or her obligations to assign all such intellectual property to his or her employing institution.

Litigation may be necessary to defend against these and other claims challenging inventorship or ownership of inventions. If we are unsuccessful in defending against any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

***Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.***

The USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process. There are situations in which noncompliance can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case.

***Issued patents covering PRT-201 or covering any additional product candidates could be found invalid or unenforceable if challenged in court.***

If we initiated legal proceedings against a third party to enforce a patent, if and when issued, covering PRT-201 or any additional product candidate, the defendant could counterclaim that the patent covering our product candidate is invalid and/or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge include alleged failures to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Grounds for unenforceability assertions include allegations that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include reexamination and *inter partes* review in the United States and equivalent proceedings in foreign jurisdictions, *e.g.*, opposition proceedings. Such proceedings could result in revocation or amendment of our patents in such a way that they no longer cover, for example, PRT-201 or competitive products. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to validity, for example, we cannot be certain that there is no invalidating prior art, including prior art of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the

patent protection on the applicable product candidate. Such a loss of patent protection would have a material adverse impact on our business.

***We will not seek to protect our intellectual property rights in all jurisdictions throughout the world and we may not be able to adequately enforce our intellectual property rights even in the jurisdictions where we seek protection.***

Filing, prosecuting and defending patents on product candidates in all countries and jurisdictions throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States could be less extensive than those in the United States, assuming that rights are obtained in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions.

Competitors may use our technologies in jurisdictions where we do not pursue and obtain patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our products and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing. Even if we pursue and obtain issued patents in particular jurisdictions, our patent claims or other intellectual property rights may not be effective or sufficient to prevent third parties from so competing.

The laws of some foreign countries do not protect intellectual property rights to the same extent as the laws of the United States. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The legal systems of some countries, particularly developing countries, do not favor the enforcement of patents and other intellectual property protection, especially those relating to biotechnology. This could make it difficult for us to stop the infringement of our patents, if obtained, or the misappropriation of our other intellectual property rights. For example, many foreign countries have compulsory licensing laws under which a patent owner must grant licenses to third parties. In addition, many countries limit the enforceability of patents against third parties, including government agencies or government contractors. In these countries, patents may provide limited or no benefit. Patent protection must ultimately be sought on a country-by-country basis, which is an expensive and time-consuming process with uncertain outcomes. Accordingly, we may choose not to seek patent protection in certain countries, and we will not have the benefit of patent protection in such countries.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, particularly those relating to biopharmaceuticals, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

***Some of our intellectual property may have been discovered through government funded programs and thus may be subject to federal regulations such as government "march-in" rights, certain reporting requirements, and a preference for United States industry. Compliance with such regulations may limit our exclusive rights, subject us to expenditure of resources with respect to reporting requirements, and limit our ability to contract with non-United States manufacturers.***

Some of our intellectual property rights may have been generated through the use of United States government funding and therefore are subject to certain federal regulations. For example, our patents relating to some therapeutic uses of PRT-201 and associated systems and kits that include a catheter, which we refer to as the "therapy family," arose from research funded by the United States government. As a result, the United States government has certain rights to this intellectual property pursuant to the Bayh-Dole Act of 1980, or Bayh-Dole Act. These United States government rights in certain inventions developed under a government-funded program include a non-exclusive, non-transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the United States government has the right to require us to grant exclusive, partially exclusive, or non-exclusive licenses to any of these inventions to a third party if it determines that: (i) adequate steps have not been taken to commercialize the invention; (ii) government action is necessary to meet public health or safety needs; or (iii) government action is necessary to meet requirements for public use under federal regulations, also referred to as "march-in rights." The United States government also has the right to take title to these inventions if we, or the applicable licensor, fail to disclose the invention to the government and fail to file an application to register the intellectual property within specified time limits. In addition, the United States government may acquire title to these inventions in any country in which a patent application is not filed within specified time limits. Intellectual property generated under a government funded program is also subject to certain reporting requirements, compliance with which may require us or the applicable licensor to expend substantial resources. In addition, the United States government requires that any products embodying the subject invention or produced through the use of the subject invention be manufactured substantially in the United States. The manufacturing preference requirement can be waived if the owner of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the United States or that under the circumstances domestic manufacture is not commercially feasible. This preference for United States manufacturers may limit our ability to contract with non-United States product manufacturers for products covered by such intellectual property.

We currently do not plan to apply for additional United States government funding, but if we do, and we discover compounds or drug or biological candidates as a result of such funding, intellectual property rights to such discoveries may be subject to the applicable provisions of the Bayh-Dole Act.

***If we do not obtain additional protection under the Hatch-Waxman Amendments and similar foreign legislation by extending the patent protection for PRT-201, our business may be materially harmed.***

Depending upon the timing, duration and specifics of the first FDA marketing approval of PRT-201 and, if applicable, any additional product candidates, a United States patent that we own or license may be eligible for limited patent term restoration under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit extension of patent protection for up to five years as compensation for patent term lost during product development and the FDA regulatory review process. During this period of extension, the scope of protection is limited to the approved product for approved uses (for patents claiming a product) and any use claimed by the patent and approved for the product (for patents claiming a method of using a product).

Although we plan on seeking patent term restoration for our products, it may not be granted if, for example, we fail to apply within applicable deadlines, fail to apply prior to expiration of relevant patents or otherwise fail to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term restoration or the term of any such patent restoration is less than we request, our competitors may be able to enter the market and compete against us sooner than we anticipate, and our ability to generate revenues could be materially adversely affected.

***Changes in United States patent law could diminish the value of patents in general, thereby impairing our ability to protect our products.***

As is the case with other biotechnology companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biotechnology industry involve both technological and legal complexity, and is therefore costly, time-consuming and inherently uncertain. In addition, the United States has recently enacted and is currently implementing wide-ranging patent reform legislation: the Leahy-Smith America Invents Act. The America Invents Act includes a number of significant changes to United States patent law. These include provisions that affect the way patent applications will be prosecuted, provides expanded opportunities for post-grant administrative review of patents before the USPTO, and may also affect patent litigation. It is not yet clear what, if any, impact the America Invents Act will have on the operation of our business. However, the America Invents Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of any patents that may issue from our patent applications, all of which could have a material adverse effect on our business and financial condition.

In addition, recent United States Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. The full impact of these decisions is not yet known. For example, on March 20, 2012 in *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, the Court held that several claims drawn to measuring drug metabolite levels from patient samples and correlating them to drug doses were not patent-eligible subject matter. The decision appears to impact diagnostics patents that merely apply a law of nature via a series of routine steps and it has created uncertainty around the ability to obtain patent protection for certain inventions. Additionally, on June 13, 2013 in *Association for Molecular Pathology v. Myriad Genetics, Inc.*, the Court held that claims to isolated genomic DNA are not patent-eligible, but claims to complementary DNA molecules are patent-eligible because they are not a natural product. The effect of the decision on patents for other isolated natural products is uncertain. However, on March 4, 2014, the USPTO issued a memorandum to patent examiners providing guidance for examining claims that recite laws of nature, natural phenomena or natural products under the *Myriad* and *Prometheus* decisions. This guidance did not limit the application of *Myriad* to DNA but, rather, applied the decision to other natural products.

In addition to increasing uncertainty with regard to our ability to obtain future patents, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on these and other decisions by the United States Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our current or future patents.

***We may be subject to damages resulting from claims that we or our employees have wrongfully used or disclosed alleged trade secrets of their former employers.***

Our employees have been previously employed at other biotechnology or pharmaceutical companies, including our competitors or potential competitors, or at universities or academic medical centers. We also engage advisors and consultants who are concurrently employed at universities or who perform services for other entities. Although we are not aware of any claims currently pending against us, we may be subject to

claims that we or our employees, advisors or consultants have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of a former employer or other third party. We may in the future also be subject to claims that an employee, advisor or consultant performed work for us that conflicts with that person's obligations to a third party, such as an employer, and thus, that the third party has an ownership interest in the intellectual property arising out of work performed for us. Litigation may be necessary to defend against these claims. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management. If we are unsuccessful in defending against such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. A loss of key personnel or their work product could hamper or prevent our ability to commercialize PRT-201 or any additional product candidates, which would materially adversely affect our commercial development efforts.

***Numerous factors may limit any potential competitive advantage provided by our intellectual property rights.***

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business, provide a barrier to entry against our competitors or potential competitors, or permit us to maintain our competitive advantage. Moreover, if a third party has intellectual property rights that cover the practice of our technology, we may not be able to exercise or extract value from our intellectual property rights fully or at all. The following examples are illustrative:

- we might not have been the first to make the inventions covered by a patent or pending patent application that we own;
- we might not have been the first to file patent applications covering an invention;
- others may independently develop similar or alternative technologies without infringing our intellectual property rights;
- third parties may compete with us in jurisdictions where we do not pursue and obtain patent protection;
- pending patent applications that we own may not lead to issued patents;
- patents that we own may not provide us with any competitive advantages, or may be held invalid or unenforceable;
- third parties may assert an ownership interest in our intellectual property;
- we may not develop or in-license additional proprietary technologies that are patentable; and
- the patents or proprietary rights of others may have an adverse effect on our business.

Should any of these events occur, they could significantly harm our business and results of operations.

**Risks Related to Our Business and Industry**

***If we fail to attract and keep senior management and key scientific personnel, we may be unable to successfully develop our products, conduct our clinical trials and commercialize our product candidates.***

Our future growth and success depend on our ability to recruit, retain, manage and motivate our employees. We are highly dependent on our senior management team, in particular, Timothy Noyes, our President and Chief Executive Officer, Steven Burke, our Senior Vice President and Chief Medical Officer, George Eldridge, our Senior Vice President, Chief Financial Officer, Treasurer and Secretary and Daniel Gottlieb, our Vice President, Marketing and Business Development, as well as the other principal members of our management and scientific teams. Although we have formal employment agreements with our executive officers, these agreements do not prevent them from terminating their employment with us at any time. The loss of the services of any member of our senior management or scientific team or the inability to hire or retain experienced management personnel could adversely affect our ability to execute our business plan and harm our operating results.

Because of the specialized scientific and managerial nature of our business, we rely heavily on our ability to attract and retain qualified scientific, technical and managerial personnel. We do not currently carry "key person" insurance on the lives of members of executive management. The competition for qualified personnel in the pharmaceutical field is intense. Due to this intense competition, we may be unable to continue to attract and retain qualified personnel necessary for the development of our business or to recruit suitable replacement personnel. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy including, F. Nicholas Franano, our scientific founder. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us.

***We will need to significantly increase the size of our organization, and we may experience difficulties in managing growth.***

We are currently a small company with 11 full-time employees and one part-time employee as of March 31, 2014. In order to commercialize our potential products, we will need to increase our operations and expand our use of our third-party contractors. We plan to continue to build our compliance, financial and operating infrastructure to ensure the maintenance of a well-managed company including hiring additional staff within our regulatory and clinical groups after Phase 3 is complete. We intend to recruit an in-house commercial organization in the United States focused on promoting PRT-201, if it is approved. We currently do not have a sales and marketing capability and therefore intend to recruit a specialty hospital sales force of approximately 75-100 representatives in anticipation of PRT-201's approval. We will need to expand our employment base when we are in the full commercial stages of our current potential product's life cycle.

Future growth will impose significant added responsibilities on members of management, including the need to identify, recruit, maintain and integrate additional employees. In addition, to meet our obligations as a public company, we will need to increase our general and administrative capabilities. Our management, personnel and systems currently in place may not be adequate to support this future growth. Our future financial performance and our ability to commercialize our potential products and to compete effectively will depend, in part, on our ability to manage any future growth effectively. To that end, we must be able to:

- manage our clinical trials and the regulatory process effectively;
- manage the manufacturing of product candidates and potential products for clinical and commercial use;
- integrate current and additional management, administrative, financial and sales and marketing personnel;
- develop a marketing and sales infrastructure;
- hire new personnel necessary to effectively commercialize PRT-201 and any additional product candidates;
- develop our administrative, accounting and management information systems and controls; and
- hire and train additional qualified personnel.

Product candidates that we may acquire or develop in the future may be intended for patient populations that are large. In order to continue development and marketing of these product candidates, if approved, we would need to significantly expand our operations. Our staff, financial resources, systems, procedures or controls may be inadequate to support our operations and our management may be unable to manage successfully future market opportunities or our relationships with customers and other third parties.

***Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.***

Upon completion of this offering, we will become subject to the periodic reporting requirements of the Securities Exchange Act of 1934, as amended, or the Exchange Act. Our disclosure controls and procedures are designed to reasonably assure that information required to be disclosed by us in reports we file or submit under the Exchange Act is accumulated and communicated to management, and recorded, processed, summarized and reported within the time periods specified in the rules and forms of the Securities and Exchange Commission, or SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met.

These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected.

***If product liability lawsuits are successfully brought against us, our insurance may be inadequate and we may incur substantial liability.***

We face an inherent risk of product liability claims as a result of the clinical testing of PRT-201 or any additional product candidates. We will face an even greater risk if we commercially sell PRT-201 or any additional product candidate that we develop. We maintain primary product liability insurance and excess product liability insurance that cover our clinical trials, and we plan to maintain insurance against product liability lawsuits for commercial sale of our potential products. Historically, the potential liability associated with product liability lawsuits for pharmaceutical products has been unpredictable. Although we believe that our current insurance is a reasonable estimate of our potential liability and represents a commercially reasonable balancing of the level of coverage as compared to the cost of the insurance, we may be subject to claims in connection with our clinical trials and, in the future, commercial use of our potential products, for which our insurance coverage may not be adequate, and the cost of any product liability litigation or other proceeding, even if resolved in our favor, could be substantial.

For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during clinical testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability or a breach of warranties. Large judgments have been awarded in class action lawsuits based on drugs or biologics that had unanticipated adverse effects. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of PRT-201 or any additional product candidates. Regardless of the merits or eventual outcome, liability claims may result in:

- reduced resources of our management to pursue our business strategy;
- decreased demand for our product candidates or products that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- termination of clinical trial sites or entire trial programs;
- initiation of investigations by regulators;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- significant costs to defend resulting litigation;
- diversion of management and scientific resources from our business operations;
- substantial monetary awards to trial participants or patients;
- loss of revenue; and
- the inability to commercialize any products that we may develop.



We will need to increase our insurance coverage if and when we begin selling PRT-201 or any additional product candidates if and when they receive marketing approval. However, the product liability insurance we will need to obtain in connection with the commercial sales of PRT-201 or any additional product candidates if and when they receive regulatory approval may be unavailable in meaningful amounts or at a reasonable cost. In addition, insurance coverage is becoming increasingly expensive. If we are unable to obtain or maintain sufficient insurance coverage at an acceptable cost or to otherwise protect against potential product liability claims, it could prevent or inhibit the development and commercial production and sale of PRT-201 or any additional product candidates if and when they obtain regulatory approval, which could materially adversely affect our business, financial condition, results of operations, cash flows and prospects.

Additionally, we do not carry insurance for all categories of risk that our business may encounter. Some of the policies we currently maintain include general liability, employment practices liability, property, auto, workers' compensation, products liability and directors' and officers' insurance. We do not know, however, if we will be able to maintain insurance with adequate levels of coverage. Any significant uninsured liability may require us to pay substantial amounts, which would materially adversely affect our financial position, cash flows and results of operations.

***If we engage in acquisitions in the future, we will incur a variety of costs and we may never realize the anticipated benefits of such acquisitions.***

We may attempt to acquire businesses, technologies, services, products or product candidates in the future that we believe are a strategic fit with our business. We have no present agreement regarding any material acquisitions. If we do undertake any acquisitions, however, the process of integrating an acquired business, technology, service, products or product candidates into our business may result in unforeseen operating difficulties and expenditures, including diversion of resources and management's attention from our core business. In addition, we may fail to retain key executives and employees of the companies we acquire, which may reduce the value of the acquisition or give rise to additional integration costs. Future acquisitions could result in additional issuances of equity securities that would dilute the ownership of existing stockholders. Future acquisitions could also result in the incurrence of debt, actual or contingent liabilities or the amortization of expenses related to other intangible assets, any of which could adversely affect our operating results. In addition, we may fail to realize the anticipated benefits of any acquisition.

***We currently have our active pharmaceutical ingredient, or API, produced for us by a contract manufacturer exclusively in one manufacturing facility and if this or any future facility, any facility we use for storage of the finished product or our equipment were damaged or destroyed, our ability to continue to operate our business would be materially harmed.***

Our executive offices are located at 200 Waltham, Massachusetts, and our API is manufactured at Lonza's facility located at Visp, Switzerland. We expect that Lonza plans to utilize this facility in the future to support commercial production if our product candidate is approved. We have manufactured all our finished product for the planned Phase 3 clinical trials of PRT-201 and currently store the finished product in only one location. Extended delays in our Phase 3 clinical trials causing us to need to manufacture new clinical supply would cause a significant disruption in our operations and cause us to incur unexpected costs to manufacture new finished product. We are vulnerable to natural disasters, such as severe storms and other events that could disrupt our operations. We do not carry insurance for natural disasters and we may not carry sufficient business interruption insurance to compensate us for losses that may occur. If the current manufacturing facility or any future facility, stored product or equipment were damaged or destroyed, or if we experience a significant disruption in our operations for any reason, our ability to continue to operate our business would be materially harmed.

If supply is interrupted, there could be a significant disruption in our clinical development and commercial supply. If the supply is interrupted after approval of the BLA, an alternative manufacturer

would need to be qualified through a BLA supplement which could result in further delay. The regulatory agencies may also require additional studies if a new manufacturer is relied upon for commercial production. Switching manufacturers may involve substantial costs and would likely result in a delay in our desired clinical and commercial timelines.

These factors could cause the delay of clinical trials, regulatory submissions, required approvals or commercialization of PRT-201 or any additional product candidates, cause us to incur higher costs and prevent us from commercializing our products successfully. Furthermore, if our suppliers fail to meet contractual requirements, and we are unable to secure one or more replacement suppliers capable of production at a substantially equivalent cost, our clinical trials may be delayed or we could lose potential revenue.

***Our business and operations would suffer in the event of system failures.***

Despite the implementation of security measures, our internal computer systems, and those of our CROs and other third parties on which we rely, are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. If issues were to arise and cause interruptions in our operations, it could result in a material disruption of our drug and biologic development programs. For example, the loss of clinical trial data from completed or ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of or damage to our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development of PRT-201 or any additional product candidates could be delayed.

***Our employees may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements and insider trading, which could significantly harm our business.***

We are exposed to the risk of employee fraud or other misconduct. Misconduct by employees could include intentional failures to comply with the regulations of the FDA and non-United States regulators, provide accurate information to the FDA and non-United States regulators, comply with healthcare fraud and abuse laws and regulations in the United States and abroad, and report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. We intend to adopt a code of conduct prior to completion of this offering, but it is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

***Recent federal legislation may increase the difficulty and cost for us to commercialize PRT-201 affect the prices we may obtain, and impair our ability to profitably sell PRT-201, if approved.***

In the United States and some foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval for PRT-201, restrict or regulate post-approval activities and affect our ability to profitably sell PRT-201, if approved. Legislative and regulatory proposals have been made to expand

post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We do not know whether additional legislative changes will be enacted, or whether the FDA regulations, targets or interpretations will be changed, or what the impact of such changes on the marketing approvals of PRT-201, if any, may be. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

In the United States, the pharmaceutical industry has been significantly affected by legislative initiatives. For example, the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for drug purchases by the elderly and introduced a new reimbursement methodology based on average sales prices for drugs. Cost reduction initiatives and other provisions of this legislation could decrease the coverage of, or the reimbursement rate that we receive for, PRT-201, if approved, and could seriously harm our business. While the MMA applies only to reimbursement of drugs under the Medicare program, private payors often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates, and any reduction in reimbursement that results from the MMA may result in a similar reduction in payments from non-governmental payors.

In March 2010, President Obama signed the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act of 2010 or, collectively, the Affordable Care Act, which substantially changes the way healthcare will be financed by both governmental and private insurers, and significantly impacts the pharmaceutical industry. Among the provisions of the Affordable Care Act of importance to our business, including, without limitation, our ability to commercialize, and the prices we may obtain for, PRT-201, if approved for sale, are the following:

- an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs;
- increases in the statutory minimum rebates a manufacturer must pay as a condition to having a drug available for coverage under the Medicaid program;
- expansion of healthcare fraud and abuse laws, including the federal False Claims Act and the federal Anti-Kickback Statute, and the addition of new government investigative powers and enhanced penalties for non-compliance;
- extension of a manufacturer's Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to additional individuals and by adding new eligibility categories for certain individuals with income at or below 133% of the federal poverty level beginning in 2014, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- new requirements under the federal Open Payments program and its implementing regulations;
- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

In addition, other legislative changes have been proposed and adopted since the Affordable Care Act was enacted. These changes include aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013. In January 2013, President Obama signed into law the American Taxpayer Relief Act of 2012, which, among other things, reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. The full impact on our business of the Affordable Care

Act and other new laws is uncertain but may result in additional reductions in Medicare and other healthcare funding. Nor is it clear whether other legislative changes will be adopted, if any, or how such changes would affect the demand for PRT-201, if approved.

***Governments outside the United States tend to impose strict price controls, which may adversely affect our revenues, if any.***

In international markets, reimbursement and health care payment systems vary significantly by country, and many countries have instituted price ceilings on specific products and therapies. In some countries, particularly the countries of the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain coverage and reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. There can be no assurance that our products will be considered cost-effective by third-party payors, that an adequate level of reimbursement will be available or that the third-party payors' reimbursement policies will not adversely affect our ability to sell our products profitably. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed, possibly materially.

#### **Risks Related to Our Common Stock and This Offering**

***We are an "emerging growth company" and as a result of the reduced disclosure and governance requirements applicable to emerging growth companies, our common stock may be less attractive to investors.***

We are an "emerging growth company" as defined in the JOBS Act, and we intend to take advantage of certain exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including: not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

We may take advantage of these reporting exemptions until we are no longer an emerging growth company. We will remain an emerging growth company until the earlier of (1) the last day of the fiscal year (a) following the fifth anniversary of the completion of this offering, (b) in which we have total annual gross revenue of at least \$1 billion, or (c) in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds \$700 million as of June 30th of such fiscal year, and (2) the date on which we have issued more than \$1 billion in non-convertible debt during the prior three-year period.

We have taken advantage of reduced reporting burdens in this prospectus. In particular, in this prospectus, we have provided only two years of audited financial statements and have not included all of the executive compensation related information that would be required if we were not an emerging growth company. We cannot predict whether investors will find our common stock less attractive if we rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile. In addition, the JOBS Act provides that an emerging growth company can take advantage of an extended transition period for complying with new or revised accounting standards. This allows an emerging growth company to delay the adoption of these accounting standards until they would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this exemption and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

Even after we no longer qualify as an emerging growth company, we may still qualify as a "smaller reporting company" which would allow us to take advantage of many of the same exemptions from disclosure requirements, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act and reduced disclosure obligations regarding executive compensation in this prospectus and our periodic reports and proxy statements. We cannot predict if investors will find our common stock less attractive because we will rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

***There has been no public market for our common stock prior to this offering, and you may not be able to resell our shares at or above the price you paid, or at all.***

Prior to this offering, there has been no public market for our common stock. We intend to apply to list our common stock on The NASDAQ Global Market, or NASDAQ, but an active trading market for our common stock may never develop or be sustained following this offering. If an active trading market for our common stock does not develop after this offering, the market price and liquidity of our common stock will be materially and adversely affected. You may not be able to sell your shares quickly or at the market price if trading in our common shares is not active. The offering price for our common stock will be determined by negotiations between us and the underwriters and may bear no relationship to the market price for our common stock after this offering. An active trading market for our common stock may not develop and the market price of our common stock may decline below the offering price. Further, an inactive market may also impair our ability to raise capital by selling shares of our common stock and may impair our ability to enter into strategic partnerships or acquire companies or products by using our shares of common stock as consideration.

***The market price for our common stock may be volatile, which could contribute to the loss of your investment.***

Fluctuations in the price of our common stock could contribute to the loss of all or part of your investment. Prior to this offering, there has not been a public market for our common stock. Accordingly, the initial public offering price for the shares of our common stock may not be indicative of the price that will prevail in the trading market, if any, that develops following this offering. If an active market for our common stock develops and continues, the trading price of our common stock following this offering is likely to be highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. Any of the factors listed below could have a material adverse effect on your investment in our common stock and our common stock may trade at prices significantly below the initial public offering price. In such circumstances the trading price of our common stock may not recover and may experience a further decline.

Factors affecting the trading price of our common stock may include:

- our failure to develop and commercialize PRT-201 or any additional product candidates;
- actual or anticipated fluctuations in our quarterly financial results or the quarterly financial results of companies perceived to be similar to us;
- changes in the market's expectations about our operating results;
- adverse results or delays in preclinical studies or clinical trials;
- our decision to initiate a clinical trial, not to initiate a clinical trial or to terminate an existing clinical trial;
- adverse regulatory decisions, including failure to receive regulatory approval for PRT-201 or any additional product candidates;
- success of competitive products;
- adverse developments concerning our collaborations and our manufacturers;
- inability to obtain adequate product supply for any product candidate for clinical trials or commercial sale or inability to do so at acceptable prices;

- the termination of a collaboration or the inability to establish additional collaborations;
- unanticipated serious safety concerns related to the use of any of PRT-201 or any additional product candidates;
- our ability to effectively manage our growth;
- the size and growth, if any, of the targeted market;
- our operating results failing to meet the expectation of securities analysts or investors in a particular period or failure of securities analysts to publish reports about us or our business;
- changes in financial estimates and recommendations by securities analysts concerning our company, our market opportunity, or the biotechnology and pharmaceutical industries in general;
- operating and stock price performance of other companies that investors deem comparable to us;
- overall performance of the equity markets;
- announcements by us or our competitors of acquisitions, new product candidates or programs, significant contracts, commercial relationships or capital commitments;
- our ability to successfully market PRT-201 or any additional product candidates;
- changes in laws and regulations affecting our business, including but not limited to clinical trial requirements for approvals;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for PRT-201 or any additional product candidates;
- commencement of, or involvement in, litigation involving our company, our general industry, or both;
- changes in our capital structure, such as future issuances of securities or the incurrence of additional debt;
- the volume of shares of our common stock available for public sale;
- additions or departures of key scientific or management personnel;
- any major change in our board or management;
- changes in accounting practices;
- ineffectiveness of our internal control over financial reporting;
- sales of substantial amounts of common stock by our directors, executive officers or significant stockholders or the perception that such sales could occur; and
- general economic and political conditions such as recessions, interest rates, fuel prices, international currency fluctuations and acts of war or terrorism.

Broad market and industry factors may materially harm the market price of our common stock irrespective of our operating performance. The stock market in general, and NASDAQ and the market for biotechnology companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of the particular companies affected. The trading prices and valuations of these stocks, and of ours, may not be predictable. A loss of investor confidence in the market for technology or software stocks or the stocks of other companies which investors perceive to be similar to us, the opportunities in the digital simulation market or the stock market in general, could depress our stock price regardless of our business, prospects, financial conditions or results of operations.

***Raising additional funds through debt or equity financing could be dilutive and may cause the market price of our common stock to decline.***

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings and debt financings, and potentially through license and development agreements with strategic partnerships with third parties. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of those securities could result in substantial dilution for our current stockholders and the terms may include liquidation or other preferences that adversely affect the rights of our current stockholders. Furthermore, the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our common stock to decline and existing stockholders may not agree with our financing

plans or the terms of such financings. Moreover, the incurrence of debt financing could result in a substantial portion of our operating cash flow being dedicated to the payment of principal and interest on such indebtedness and could impose restrictions on our operations, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. Additional funding may not be available to us on acceptable terms, or at all.

***If securities analysts do not publish research or reports about our business or if they downgrade our stock, the price of our common stock could decline.***

The trading market for our common stock will rely in part on the research and reports that industry or financial analysts publish about us, our business, our markets and our competitors. We do not control these analysts. If securities analysts do not cover our common stock after the closing of this offering, the lack of research coverage may adversely affect the market price of our common stock. Furthermore, if one or more of the analysts who do cover us downgrade our stock or if those analysts issue other unfavorable commentary about us or our business, our stock price would likely decline. If one or more of these analysts cease coverage of us or fails to regularly publish reports on us, we could lose visibility in the market and interest in our stock could decrease, which in turn could cause our stock price or trading volume to decline and may also impair our ability to expand our business with existing customers and attract new customers.

***The concentration of our capital stock ownership with insiders upon the closing of this offering will likely limit your ability to influence corporate matters.***

We anticipate that our executive officers, employees, directors, current 5% or greater stockholders, and their respective affiliates will together beneficially own or control, in aggregate, approximately % of the shares of our outstanding common stock, after giving effect to the conversion of all outstanding preferred stock and assuming no exercise of outstanding options or warrants following the closing of this offering (assuming no exercise of the underwriters' option to purchase additional shares). As a result, these executive officers, directors and principal stockholders, acting together, will have substantial influence over most matters that require approval by our stockholders, including the election of directors, any merger, consolidation or sale of all or substantially all or of our assets or any other significant corporate transaction. Corporate action might be taken even if other stockholders, including those who purchase shares in this offering, oppose such action. These stockholders may delay or prevent a change of control or otherwise discourage a potential acquirer from attempting to obtain control of our company, even if such change of control would benefit our other stockholders. This concentration of stock ownership may adversely affect investors' perception of our corporate governance or delay, prevent or cause a change in control of our company, any of which could adversely affect the market price of our common stock.

***Sales of a substantial number of shares of our common stock by our existing stockholders in the public market may cause our stock price to decline.***

Sales of our common stock in the public market after this offering, or the perception that these sales may occur, could cause the market price of our common stock to decline. Based on our shares of common stock outstanding as of March 31, 2014, upon the closing of this offering, we will have shares of common stock outstanding, assuming no exercise of the underwriters' over-allotment option. Of these, only the shares of our common stock sold in this offering, plus any shares sold upon exercise of the underwriters' over-allotment option, will be freely transferable without restriction or additional registration under the Securities Act of 1933, as amended, or the Securities Act. The remaining shares outstanding after this offering will be available for sale, upon the expiration of the 180-day lock-up period beginning from the date of this prospectus, if applicable, subject to volume and other restrictions as applicable under Rule 144 under the Securities Act. Any or all of these shares may be released prior to expiration of the lock-up period at the discretion of the lead underwriter for this offering. After the lock-up agreements expire, up to an additional shares of common stock will be eligible for sale in the public market, of which shares are held by directors, executive officers and other affiliates and

will be subject to volume limitations under Rule 144 under the Securities Act, assuming an initial public offering price of \$ \_\_\_\_\_ per share (the midpoint of the price range set forth on the cover page of this prospectus). In addition, \_\_\_\_\_ shares of common stock that are either subject to outstanding options or reserved for future issuance under our employee benefit plans will become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules, the lock-up agreements and Rule 144 and Rule 701 under the Securities Act. To the extent these shares are sold, or if it is perceived that they will be sold, into the market, the market price of our common stock could decline. For a further description of the dilution that you will experience immediately after this offering, see the section entitled "Share Eligible for Future Sale."

***Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our equity incentive plans, could result in additional dilution of the percentage ownership of our stockholders and could cause our stock price to fall.***

We expect that significant additional capital will be needed in the future to continue our planned operations, including conducting clinical trials, commercialization efforts, expanded research and development activities and costs associated with operating a public company. To raise capital, we may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. Such sales may also result in material dilution to our existing stockholders, and new investors could gain rights, preferences and privileges senior to the holders of our common stock, including shares of common stock sold in this offering.

***You will experience immediate and substantial dilution in the net tangible book value of the shares you purchase in this offering.***

If you purchase shares of our common stock in this offering, you will experience immediate and substantial dilution, as the initial public offering price of our common stock will be substantially greater than the net tangible book value per share of our common stock. Based on an initial offering price of \$ \_\_\_\_\_ per share, which is the midpoint of the range on the cover page of this prospectus, if you purchase our common stock in this offering, you will suffer immediate and substantial dilution of approximately \$ \_\_\_\_\_ per share. Further, investors purchasing common stock in this offering will contribute approximately \_\_\_\_\_ % of the total amount invested by stockholders since our inception, but will own only approximately \_\_\_\_\_ % of the shares of common stock outstanding after giving effect to this offering. If the underwriters exercise their over-allotment option, or if outstanding options and warrants to purchase our common stock are exercised, you will experience additional dilution. For a further description of the dilution that you will experience immediately after this offering, see the section entitled "Dilution."

***We have broad discretion in the use of net proceeds from this offering and may not use them effectively.***

We currently intend to use the net proceeds from this offering to fund the continued development of PRT-201 and for working capital and other general corporate purposes, including funding the costs of operating a public company. We may also use the proceeds to acquire and develop other products, including other drugs and biologics. For a further description of our use of proceeds from this offering, see the section entitled "Use of Proceeds." Any remaining amounts will be used for general corporate purposes, general and administrative expenses, capital expenditures, working capital and prosecution and maintenance of our intellectual property. Although we currently intend to use the net proceeds from this offering in such a manner, we will have broad discretion in the application of the net proceeds. Our failure to apply these funds effectively could affect our ability to continue to develop and commercialize our product candidate.



***We will incur significant increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives.***

As a newly public company, we will incur significant legal, accounting and other expenses that we did not incur as a private company. In addition, the Sarbanes-Oxley Act, and rules of the SEC and those of NASDAQ have imposed various requirements on public companies including requiring establishment and maintenance of effective disclosure and financial controls. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations have increased and will continue to increase our legal and financial compliance costs and will make some activities more time-consuming and costly.

The Sarbanes-Oxley Act requires, among other things, that we maintain effective internal control over financial reporting and disclosure controls and procedures. In particular, we must perform system and process evaluation and testing of our internal control over financial reporting to allow management to report on the effectiveness of our internal control over financial reporting, as required by Section 404 of the Sarbanes-Oxley Act. In addition, we will be required to have our independent registered public accounting firm attest to the effectiveness of our internal control over financial reporting the later of our second annual report on Form 10-K or the first annual report on Form 10-K following the date on which we are no longer an emerging growth company. Our compliance with Section 404 of the Sarbanes-Oxley Act will require that we incur substantial accounting expense and expend significant management efforts. We currently do not have an internal audit group, and we will need to hire additional accounting and financial staff with appropriate public company experience and technical accounting knowledge. If we are not able to comply with the requirements of Section 404 in a timely manner, or if we or our independent registered public accounting firm identify deficiencies in our internal control over financial reporting that are deemed to be material weaknesses, the market price of our stock could decline and we could be subject to sanctions or investigations by NASDAQ, the SEC or other regulatory authorities, which would require additional financial and management resources.

Our ability to successfully implement our business plan and comply with Section 404 requires us to be able to prepare timely and accurate financial statements. We expect that we will need to continue to improve existing, and implement new operational and financial systems, procedures and controls to manage our business effectively. Any delay in the implementation of, or disruption in the transition to, new or enhanced systems, procedures or controls, may cause our operations to suffer and we may be unable to conclude that our internal control over financial reporting is effective and to obtain an unqualified report on internal controls from our auditors as required under Section 404 of the Sarbanes-Oxley Act. This, in turn, could have an adverse impact on trading prices for our common stock, and could adversely affect our ability to access the capital markets.

***We do not expect to pay any cash dividends for the foreseeable future.***

You should not rely on an investment in our common stock to provide dividend income. We do not anticipate that we will pay any cash dividends to holders of our common stock in the foreseeable future. Instead, we plan to retain any earnings to maintain and expand our operations. Accordingly, investors must rely on sales of their common stock after price appreciation, which may never occur, as the only way to realize any return on their investment. As a result, investors seeking cash dividends should not purchase our common stock.

***Our ability to use our net operating loss carryovers and certain other tax attributes may be limited.***

As described above under "—Risks Related to Our Financial Condition and Need for Additional Capital", we have incurred net losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future. Under the Internal Revenue Code of 1986, as amended, or the Code, a corporation is generally allowed a deduction for net operating losses, or NOLs, carried over from a prior taxable year. Under that provision, we can carry forward our NOLs to offset our future taxable income, if any, until such NOLs are used or expire. The same is true of other unused tax attributes, such as

tax credits. The amounts of our unused carryovers of NOLs and tax credits as of December 31, 2013, and a description of the valuation allowance we have recorded with respect to those items, are set forth below under "Management's Discussion and Analysis of Financial Condition and Results of Operations."

If a corporation undergoes an "ownership change," generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period, Sections 382 and 383 of the Code limit the corporation's ability to use carryovers of its pre-change NOLs, credits and certain other tax attributes to reduce its tax liability for periods after the ownership change. Our issuance of common stock pursuant to this offering may result in a limitation under Sections 382 and 383, either separately or in combination with certain prior or subsequent shifts in the ownership of our common stock. As a result, our ability to use carryovers of our pre-change NOLs and credits to reduce our future U.S. federal income tax liability may be subject to limitations. This could result in increased U.S. federal income tax liability for us if we generate taxable income in a future period. Limitations on the use of NOLs and other tax attributes could also increase our state tax liability. The use of our tax attributes will also be limited to the extent that we do not generate positive taxable income in future tax periods.

***We could be subject to securities class action litigation.***

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biotechnology companies have experienced significant stock price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

***Provisions in our restated certificate of incorporation, our amended and restated bylaws and Delaware law may have anti-takeover effects that could discourage an acquisition of us by others, even if an acquisition would be beneficial to our stockholders, and may prevent attempts by our stockholders to replace or remove our current management.***

Our restated certificate of incorporation, amended and restated bylaws and Delaware law contain provisions that may have the effect of delaying or preventing a change in control of us or changes in our management. Our restated certificate of incorporation and bylaws include provisions that:

- authorize "blank check" preferred stock, which could be issued by our board of directors without stockholder approval and may contain voting, liquidation, dividend and other rights superior to our common stock;
- create a classified board of directors whose members serve staggered three-year terms;
- specify that special meetings of our stockholders can be called only by our board of directors;
- prohibit stockholder action by written consent;
- establish an advance notice procedure for stockholder approvals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our board of directors;
- provide that our directors may be removed only for cause;
- provide that vacancies on our board of directors may be filled only by a majority of directors then in office, even though less than a quorum;
- specify that no stockholder is permitted to cumulate votes at any election of directors;
- expressly authorize our board of directors to modify, alter or repeal our amended and restated bylaws; and
- require supermajority votes of the holders of our common stock to amend specified provisions of our restated certificate of incorporation and amended and restated bylaws.

These provisions, alone or together, could delay or prevent hostile takeovers and changes in control or changes in our management.

In addition, because we are incorporated in the state of Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which limits the ability of stockholders owning in excess of 15% of our outstanding voting stock to merge or combine with us.

Any provision of our restated certificate of incorporation or amended and restated bylaws or Delaware law that has the effect of delaying or deterring a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock, and could also affect the price that some investors are willing to pay for our common stock.

Our restated certificate of incorporation designates the Court of Chancery of the State of Delaware and federal court within the State of Delaware as the exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our restated certificate of incorporation provides that, subject to limited exceptions, the Court of Chancery of the State of Delaware and federal court within the State of Delaware will be exclusive forums for (1) any derivative action or proceeding brought on our behalf, (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or other employees to us or our stockholders, (3) any action asserting a claim against us arising pursuant to any provision of the Delaware General Corporation Law, our restated certificate of incorporation or our amended and restated bylaws, or (4) any other action asserting a claim against us that is governed by the internal affairs doctrine. Any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock shall be deemed to have notice of and to have consented to the provisions of our restated certificate of incorporation described above. This choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits against us and our directors, officers and employees. Alternatively, if a court were to find these provisions of our restated certificate of incorporation inapplicable to, or unenforceable in respect of, one or more of the specified types of actions or proceedings, we may incur additional costs associated with resolving such matters in other jurisdictions, which could adversely affect our business and financial condition.

## SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains forward-looking statements, which reflect our current views with respect to, among other things, our operations and financial performance. You can identify these forward-looking statements by the use of words such as "outlook," "believes," "expects," "potential," "continues," "may," "will," "should," "seeks," "approximately," "predicts," "intends," "plans," "estimates," "anticipates" or the negative version of these words or other comparable words. These forward-looking statements are subject to various risks and uncertainties. Accordingly, there are or will be important factors that could cause actual outcomes or results to differ materially from those indicated in these statements. We believe these factors include but are not limited to those described under "Risk Factors" and include, among other things:

- the timing of results of our ongoing and planned clinical trials for PRT-201;
- our estimates regarding the amount of funds we require to complete our two planned Phase 3 clinical trials for PRT-201;
- our estimate of when we will require additional funding;
- our plans to commercialize PRT-201;
- the timing of, and our ability to, obtain and maintain regulatory approvals for our product candidates;
- the rate and degree of market acceptance and clinical utility of any approved product candidate;
- the potential benefits of strategic partnership agreements and our ability to enter into selective strategic partnership arrangements;
- our ability to quickly and efficiently identify and develop product candidates;
- our commercialization, marketing and manufacturing capabilities and strategy;
- our intellectual property position; and
- our estimates regarding expenses, future revenues, capital requirements, the sufficiency of our current and expected cash resources and our need for additional financing.

These factors should not be construed as exhaustive and should be read in conjunction with the other cautionary statements that are included in this prospectus. We undertake no obligation to publicly update or review any forward-looking statement, whether as a result of new information, future developments or otherwise.

## USE OF PROCEEDS

We estimate that our net proceeds from this offering will be approximately \$ \_\_\_\_\_ million, assuming an initial public offering price of \$ \_\_\_\_\_ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters exercise their option to purchase additional shares in full, we estimate that our net proceeds from this offering will be approximately \$ \_\_\_\_\_ million.

Each \$1.00 increase or decrease in the assumed initial public offering price of \$ \_\_\_\_\_ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, would result in an approximately \$ \_\_\_\_\_ million increase or decrease in our net proceeds from this offering, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. Each increase or decrease of one million shares in the number of shares to be offered by us would increase or decrease our net proceeds from this offering by approximately \$ \_\_\_\_\_ million, assuming that the public offering price is \$ \_\_\_\_\_ per share, the midpoint of the price range set forth on the cover page of this prospectus and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

We expect to use the net proceeds of this offering as follows:

- approximately \$ \_\_\_\_\_ million to accelerate the commencement of the second of our Phase 3 trials for PRT-201 in its lead indication;
- approximately \$ \_\_\_\_\_ million to accelerate our chemistry and manufacturing controls, or CMC, activities;
- approximately \$ \_\_\_\_\_ million to fund additional research and development activities, including preliminary clinical work for additional indications; and
- the remainder for working capital and general corporate purposes and the costs associated with being a public company.

Our expected use of net proceeds from this offering represents our intentions based upon our present plans and business conditions, which could change in the future as our plans and business conditions evolve. The amount and timing of our actual expenditures will depend upon numerous factors, including the results of our ongoing clinical trials and clinical trials that we may commence, feedback from regulatory agencies, the timing of approval of any of our product candidates, the results of any commercialization efforts and other factors. As a result, our management will have broad discretion over the use of the net proceeds from this offering.

Pending the use of the proceeds from this offering, we intend to invest the net proceeds in short-term, interest-bearing, investment-grade securities, certificates of deposit or government securities.

## DIVIDEND POLICY

We have never declared or paid any cash dividends on our common stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. We do not intend to pay cash dividends to holders of our common stock in the foreseeable future.

## CAPITALIZATION

The following table sets forth our cash and capitalization as of March 31, 2014 on:

- an actual basis;
- a pro forma basis to give effect to the automatic conversion of all outstanding shares of our preferred stock and our convertible notes outstanding and accrued interest into an aggregate of 71,449,692 shares of common stock upon the closing of this offering and the filing of our amended and restated certificate of incorporation upon the closing of this offering; and
- a pro forma as adjusted basis to give further effect to the sale of \_\_\_\_\_ shares of our common stock offered in this offering, assuming an initial public offering price of \$ \_\_\_\_\_ per share, the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

You should read this table together with the information contained in this prospectus, including "Management's Discussion and Analysis of Financial Condition and Results of Operations" and the historical financial statements and related notes included elsewhere in this prospectus.

	As of March 31, 2014		
	Actual	Pro Forma	Pro Forma as Adjusted
	(in thousands, except share and per share data)		
	\$	\$	\$
Cash and cash equivalents	3,586	3,586	—
Convertible notes, including accrued interest payable of \$198 and associated derivative liability of \$1,512 as of March 31, 2014 <sup>(1)</sup>	6,048	—	—
<b>Convertible Preferred Stock:</b>			
Series A redeemable convertible preferred stock, par value \$0.001 per share; 22,638,465 shares authorized, issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	34,624	—	—
Series A-1 redeemable convertible preferred stock, par value \$0.001 per share; 10,909,091 shares authorized, issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	17,583	—	—
Series B redeemable convertible preferred stock, par value \$0.001 per share; 20,754,461 shares authorized, issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	28,014	—	—
Series C redeemable convertible preferred stock, par value \$0.001 per share; 17,550,758 shares authorized, 13,202,932 shares issued and outstanding, actual; no shares authorized, issued or outstanding, pro forma and pro forma as adjusted	17,696	—	—
Total convertible preferred stock	97,917	—	—
<b>Stockholders' deficit:</b>			
Preferred stock, par value \$0.001 per share; no shares authorized, issued and outstanding, actual, _____ shares authorized, no shares issued and outstanding pro forma and pro forma as adjusted	—	—	—
Common stock, par value \$0.001 per share; 100,370,203 shares authorized, 3,811,106 shares issued and outstanding, actual; 100,370,203 shares authorized, 75,260,798 shares issued and outstanding, pro forma and _____ shares authorized, _____ shares issued and outstanding, pro forma as adjusted	4	76	—
Additional paid-in capital	—	102,381	—
Accumulated deficit	(104,844)	(103,332)	—
Total stockholders' deficit	(104,840)	(875)	—
Total capitalization	\$ (875)	\$ (875)	—

(1) Converted on May 13, 2014, at the initial closing of our Series D convertible preferred stock financing. See description of our Series D convertible preferred stock financing below under the heading "—Series D Convertible Preferred Stock."

Each \$1.00 increase or decrease in the assumed initial public offering price of \$ \_\_\_\_\_ per share, the mid-point of the price range set forth on the cover page of this prospectus, would increase or decrease each of cash and cash equivalents, additional paid-in capital, total stockholders' deficit and total capitalization on a pro forma as adjusted basis by approximately \$ \_\_\_\_\_ million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. Each increase or decrease of 1,000,000 shares in the number of shares offered by us would increase or decrease each of cash and cash equivalents, additional paid-in capital, total stockholders' deficit and total capitalization on a pro forma as adjusted basis by approximately \$ \_\_\_\_\_ million, assuming no change in the assumed initial public offering price of \$ \_\_\_\_\_ per share and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

The table above does not include shares of our common stock issuable upon conversion of the Series D convertible preferred stock issued after March 31, 2014, as described below under the heading "—Series D Convertible Preferred Stock—Initial issuance of Series D convertible preferred stock" and the following potentially dilutive shares of common stock outstanding at March 31, 2014:

- 9,629,620 shares of our common stock issuable upon the exercise of stock options outstanding at a weighted-average exercise price of \$0.14 per share;
- 10,471,282 shares of our common stock issuable upon the exercise of outstanding warrants at a weighted average exercise price of \$0.29 per share that we expect to be exercised in full prior to the closing of this offering;
- 255,504 shares of common stock reserved for issuance pursuant to future equity awards under our 2006 Equity Incentive Plan; and
- shares of common stock reserved for future issuance under our 2014 Equity Incentive Plan, which will become effective immediately prior to the closing of this offering (including \_\_\_\_\_ shares reserved for issuance under our 2006 Equity Incentive Plan, which will be added to the shares reserved for issuance under the 2014 Equity Incentive Plan upon its effectiveness).

### **Series D Convertible Preferred Stock**

*Initial issuance of Series D convertible preferred stock.* On May 13, 2014, we entered into a Series D Convertible Preferred Stock Purchase Agreement, or the Series D Purchase Agreement, pursuant to which (i) we sold and issued a total of 10,344,201 shares of Series D convertible preferred stock upon the conversion of approximately \$4.5 million of principal and accrued interest outstanding under convertible promissory notes at a conversion price of \$0.4414 per share, and (ii) we sold and issued 42,469,626 shares of Series D convertible preferred stock to new and existing investors for aggregate gross proceeds of \$25.0 million at a price per share of \$0.588656.

*Additional issuances of Series D convertible preferred stock.* The Series D Purchase Agreement also contemplates our sale in two additional subsequent closings, which we refer to as the second tranche and third tranche closings, of up to an additional 33,975,700 shares of our Series D convertible preferred stock. Our right to cause the second and third tranche closings to occur will terminate at the closing of this offering.

*Individual Purchase Rights after the closing of this offering.* Following the closing of this offering, the investors that are parties to the Series D Purchase Agreement will have individual purchase rights under the Series D Purchase Agreement to purchase from us, at any time and from time to time until May 13, 2024, an aggregate of \_\_\_\_\_ shares of our common stock, assuming an initial public offering price of \$ \_\_\_\_\_ per share, the midpoint of the price range set forth on the cover page of this prospectus, and assuming also that such individual purchase rights are not terminated, in whole or in part, as described below in this paragraph. The purchase price per share for common stock purchased pursuant to such

individual purchase rights will be the lower of (i) 0.588656, the Series D conversion price immediately prior to this offering and (ii) the initial public offering price. If we or our underwriters offer to the investors that are parties to the Series D Purchase Agreement the opportunity to purchase shares of common stock in this offering, which offer to purchase will be made only if so determined by us or our underwriters at the sole discretion of us or our underwriters, then the individual purchase rights under the Series D Purchase Agreement of such investors shall terminate at the closing of this offering to the extent of the number of shares of our common stock that such investors are offered the opportunity to purchase in this offering, regardless of whether such investors actually purchase any of such shares so offered in this offering. For example, if the individual purchase rights under the Series D Purchase Agreement of the investors that are parties to the Series D Purchase Agreement are exercisable to purchase from us an aggregate of \_\_\_\_\_ shares of our common stock, and if we or our underwriters offer to such investors the opportunity to purchase an aggregate of \_\_\_\_\_ shares of our common stock in this offering, then the individual purchase rights under the Series D Purchase Agreement of such investors shall terminate at the closing of this offering, regardless of whether such investors actually purchase any of the shares of our common stock that such investors are offered the opportunity to purchase in this offering. On the other hand, if, for example, the individual purchase rights under the Series D Purchase Agreement of the investors that are parties to the Series D Purchase Agreement are exercisable to purchase from us an aggregate of \_\_\_\_\_ shares of our common stock, and if we or our underwriters offer to such investors the opportunity to purchase an aggregate of only \_\_\_\_\_ shares of our common stock in this offering, then, regardless of whether such investors actually purchase any of such shares so offered in this offering, the individual purchase rights under the Series D Purchase Agreement of such investors shall terminate at the closing of this offering with respect to an aggregate of \_\_\_\_\_ shares of our common stock and shall remain exercisable, at any time and from time to time until May 13, 2024, with respect to an aggregate of \_\_\_\_\_ shares of our common stock.

*Anti-dilution protection for Series D convertible preferred stock.* At the closing of this offering, our Series D convertible preferred stock will automatically convert into a number of shares of our common stock equal to (i) \_\_\_\_\_ shares plus (ii) an incremental amount of shares. This incremental amount of shares will be applicable only if we or our underwriters offer to the holders of shares of our Series D convertible preferred stock the opportunity to purchase shares in this offering, such holders purchase shares in this offering and the initial public offering price per share is greater than \$ \_\_\_\_\_, the purchase price per share of our Series D convertible preferred stock. This incremental amount of shares will be determined by multiplying (x) the number of shares of common stock purchased in this offering by the holders of our Series D convertible preferred stock up to a maximum number of shares of our common stock equal to \_\_\_\_\_ shares, which number of shares is equal to the number of shares of our Series D convertible preferred stock that such holders would have been entitled to purchase under the Series D Purchase Agreement at the second and third tranche closings if the second and third tranche closings had been consummated prior to the closing of this offering, by (y) the remainder obtained by subtracting the number one from the quotient obtained by dividing the initial public offering price per share by \$ \_\_\_\_\_, the purchase price per share of our Series D convertible preferred stock.

Upon the closing of this offering, assuming an initial public offering price of \$ \_\_\_\_\_ per share, the midpoint of the price range set forth on the cover page of this prospectus, and assuming that none of the holders of our Series D convertible preferred stock purchase shares of our common stock in this offering, then the \_\_\_\_\_ shares of our Series D convertible preferred stock outstanding as of \_\_\_\_\_, 2014 automatically will convert into \_\_\_\_\_ shares of our common stock.

Upon the closing of this offering, assuming an initial public offering price of \$ \_\_\_\_\_ per share, the midpoint of the price range set forth on the cover page of this prospectus, and assuming that the holders of our Series D convertible preferred stock purchase in this offering an aggregate of at least \_\_\_\_\_ shares of our common stock, which number of shares is equal to the number of shares of our Series D convertible preferred stock that such holders would have been entitled to purchase under the Series D Purchase Agreement at the second and third tranche closings if the second and third tranche closings had been



consummated prior to the closing of this offering, then the \_\_\_\_\_ shares of our Series D convertible preferred stock outstanding as of \_\_\_\_\_, 2014 automatically will convert into \_\_\_\_\_ shares of our common stock. Each \$1.00 decrease in the assumed initial public offering price (until the assumed initial public offering price is equal to \$ \_\_\_\_\_) would decrease by an additional \_\_\_\_\_ shares the number of shares of our common stock that would be issued upon the conversion of our Series D convertible preferred stock at the closing of this offering. In the event of a decrease in the assumed initial public offering price to a price that is equal to or less than \$ \_\_\_\_\_, the \_\_\_\_\_ shares of our Series D convertible preferred stock outstanding as of \_\_\_\_\_, 2014 automatically will convert into \_\_\_\_\_ shares of our common stock upon the closing of this offering. Each \$1.00 increase in the assumed initial public offering price above \$ \_\_\_\_\_ would increase by an additional \_\_\_\_\_ shares the number of shares of our common stock that would be issued upon the conversion of our Series D convertible preferred stock at the closing of this offering. In the event that the assumed initial public offering price is greater than \$ \_\_\_\_\_, each decrease of \_\_\_\_\_ shares in the number of shares purchased in this offering by holders of our Series D convertible preferred stock would decrease by an additional \_\_\_\_\_ shares the number of shares of our common stock that would be issued upon the conversion of our Series D convertible preferred stock at the closing of this offering.

Since the capitalization table provided above is as of March 31, 2014, the capitalization table does not reflect the sale and issuance by us of the shares of our Series D convertible preferred stock on May 13, 2014 or our receipt of the proceeds from such sale and issuance.

## DILUTION

If you invest in our common stock in this offering, your ownership interest will be diluted immediately to the extent of the difference between the public offering price per share of our common stock and the pro forma net tangible book value per share of our common stock after this offering.

Our historical net tangible book deficit as of March 31, 2014 was \$(104.8) million or \$(27.51) per share of common stock, based on 3,811,106 shares of common stock outstanding as of March 31, 2014. Historical net tangible book value per share is determined by dividing our total tangible assets less total liabilities and redeemable preferred stock by the actual number of shares of common stock outstanding.

Our pro forma net tangible book deficit as of March 31, 2014 was \$(0.9) million, or \$(0.01) per share of common stock, based on 75,260,798 shares of common stock outstanding including 67,504,949 shares of common stock after giving effect to the automatic conversion of all of our outstanding series A, A-1, B and C convertible preferred stock and 3,944,743 shares of common stock after giving effect to the automatic conversion of our convertible notes and accrued interest upon the listing of our common stock on the NASDAQ Global Market. Pro forma net tangible book value per share is determined by dividing our total tangible assets less total liabilities and redeemable preferred stock by the pro forma number of shares of common stock outstanding at March 31, 2014 before giving effect to our sale of shares of common stock in this offering.

After giving further effect to our issuance and sale of \_\_\_\_\_ shares of our common stock in this offering at an assumed initial public offering price of \$ \_\_\_\_\_ per share, which is the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma net tangible book value as of March 31, 2014 would have been \$ \_\_\_\_\_ million, or \$ \_\_\_\_\_ per share. This represents an immediate increase in pro forma net tangible book value per share of \$ \_\_\_\_\_ to existing stockholders and immediate dilution of \$ \_\_\_\_\_ in pro forma net tangible book value per share to new investors purchasing common stock in this offering.

Dilution per share to new investors is determined by subtracting pro forma net tangible book value per share after this offering from the initial public offering price per share paid by new investors. The following table illustrates this dilution on a per share of common stock basis assuming the underwriters do not exercise their option to purchase additional shares of common stock:

Assumed initial public offering price per share	\$
Historical net tangible book value per share as of March 31, 2014	\$ (27.51)
Pro forma increase per share as of March 31, 2014 attributable to conversion of convertible preferred stock	27.50
Pro forma net tangible book value per share as of March 31, 2014 before giving effect to this offering	<u>(0.01)</u>
Increase per share attributable to this offering	<u>          </u>
Pro forma net tangible book value per share, as adjusted to give effect to this offering	<u>          </u>
Dilution in pro forma net tangible book value per share to new investors in this offering	<u>\$</u>

Each \$1.00 increase or decrease in the assumed initial public offering price of \$ \_\_\_\_\_ per share, which is the midpoint of the price range listed on the cover page of this prospectus, would increase or decrease our pro forma net tangible book value by approximately \$ \_\_\_\_\_ million, our pro forma net tangible book value per share by approximately \$ \_\_\_\_\_ and dilution per share to new investors by approximately \$ \_\_\_\_\_, assuming that the number of shares offered by us, as set forth on the cover page of

this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. We may also increase or decrease the number of shares we are offering. An increase of one million in the number of shares offered by us would increase the pro forma as adjusted net tangible book value by approximately \$            million, or \$            per share, and would decrease the dilution per share to new investors in this offering by \$            per share, assuming that the assumed initial public offering price remains the same, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses. Similarly, a decrease of one million shares in the number of shares offered by us would decrease the pro forma as adjusted net tangible book value by approximately \$            million, or \$            per share, and would increase the dilution per share to new investors in this offering by \$            per share, assuming that the assumed initial public offering price remains the same, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses. The pro forma as adjusted information discussed above is illustrative only and will adjust based on the actual initial price to the public and other terms of this offering determined at pricing.

If the underwriters exercise their option to purchase additional shares in full or if any additional shares are issued in connection with outstanding options, you will experience further dilution. If the underwriters exercise their over-allotment option in full, the following will occur:

- the percentage of shares of our common stock held by existing stockholders will decrease to approximately            % of the total number of shares of our common stock outstanding after this offering; and
- the number of shares of our common stock held by new investors will increase to, or approximately            % of the total number of shares of our common stock outstanding after this offering.

The following table summarizes, on the same pro forma basis as adjusted as of March 31, 2014, the total number of shares of common stock purchased from us, the total cash consideration paid to us and the average price per share of common stock paid by our existing owners and by new investors purchasing shares of common stock in this offering:

	Shares Purchased		Total Consideration		Average Price
	Number	Percent	Amount	Percent	Per Share
Existing stockholders			% \$		% \$
Investors participating in this offering					
<b>Total</b>		<b>100.0%</b>	<b>\$</b>	<b>100.0%</b>	

Each \$1.00 increase or decrease in the assumed public offering price of \$            per share, which is the midpoint of the price range listed on the cover page of this prospectus, would increase or decrease the total consideration paid by new investors by \$            million and increase or decrease the percentage of total consideration paid by new investors by approximately            %, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same.

The foregoing tables and calculations are based upon 75,260,798 shares of common stock outstanding as of March 31, 2014, including 67,504,949 shares of common stock after giving effect to the conversion of our outstanding series A, A-1, B and C convertible preferred stock and 3,944,743 shares of common stock after giving effect to the automatic conversion of our convertible notes and accrued interest, and excludes:

- the conversion of our series D convertible preferred stock into an aggregate of 52,813,827 shares of common stock, which series D convertible preferred stock was issued on May 13, 2014 which included the conversion of \$4.5 million of convertible notes and accrued interest into 10,344,201 shares of Series D convertible preferred stock, and which conversion is described in the section of this prospectus entitled "Capitalization—Series D Convertible Preferred Stock";

- an additional 14,599,918 shares of common stock issuable upon conversion of all of our outstanding series A, A-1, B and C convertible preferred stock, which additional shares are issuable as a result of conversion price adjustments in the anti-dilution provisions of our series A, A-1, B and C convertible preferred stock, as a result of the issue price of our series D convertible preferred stock and which is described in the section of this prospectus entitled "Capitalization—Series D Convertible Preferred Stock";
- 9,629,620 shares of our common stock issuable upon the exercise of stock options outstanding as of March 31, 2014 at a weighted-average exercise price of \$0.14 per share;
- 10,471,282 shares of our common stock issuable upon the exercise of outstanding warrants at a weighted average exercise price of \$0.29 per share;
- 255,504 shares of common stock reserved for issuance pursuant to future equity awards under our 2006 Equity Incentive Plan; and
- shares of common stock reserved for future issuance under our 2014 Equity Incentive Plan, which will become effective immediately prior to the closing of this offering (including shares of common stock reserved for issuances under our 2006 Equity Incentive Plan, which will be added to the shares reserved under the 2014 Equity Incentive Plan upon its effectiveness).

Furthermore, we may choose to raise additional capital through the sale of equity or convertible debt securities due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. New investors will experience further dilution if any of our outstanding options or warrants are exercised, new options are issued and exercised under our equity incentive plans or we issue additional shares of common stock, other equity securities or convertible debt securities for lower consideration per share than in this offering in the future.

## SELECTED FINANCIAL DATA

The selected statements of operations data for the years ended December 31, 2012 and 2013 and the balance sheet data at December 31, 2012 and 2013 have been derived from our audited financial statements included elsewhere in this prospectus. The selected statement of operations data for the three months ended March 31, 2013 and 2014 and the selected balance sheet data as of March 31, 2014 were derived from our unaudited financial statements appearing elsewhere in this prospectus. These unaudited financial statements have been prepared on a basis consistent with our audited financial statements and, in our opinion, contain all adjustments, consisting only of normal and recurring adjustments, necessary for a fair presentation of such financial data. Our historical results for any prior period are not necessarily indicative of results to be expected in any future period, and our interim period results are not necessarily indicative of results to be expected for a full year or any other interim period.

The information set forth below should be read in conjunction with the "Management's Discussion and Analysis of Financial Condition and Results of Operations" section of this prospectus and with our financial statements and notes thereto included elsewhere in this prospectus. The selected financial data in this section are not intended to replace the financial statements and are qualified in their entirety by the financial statements and related notes included elsewhere in this prospectus.

	Years Ended December 31,		Three Months Ended March 31,	
	2012	2013	2013	2014
(unaudited)				
(in thousands, except share and per share data)				
<b>Statement of Operations Data:</b>				
Operating expenses:				
Research and development	\$ 5,907	\$ 3,994	\$ 1,134	\$ 1,189
General and administrative	2,089	3,128	737	744
Total operating expenses	<u>7,996</u>	<u>7,122</u>	<u>1,871</u>	<u>1,933</u>
Loss from operations	(7,996)	(7,122)	(1,871)	(1,933)
Other income (expense):				
Investment income	20	4	2	—
Interest expense	—	(861)	—	(828)
Other income (expense)	6	67	4	(70)
Total other income (expense)	<u>26</u>	<u>(790)</u>	<u>6</u>	<u>(898)</u>
Net loss	<u>\$ (7,970)</u>	<u>\$ (7,912)</u>	<u>\$ (1,865)</u>	<u>\$ (2,831)</u>
Unrealized loss on available-for-sale investments	(5)	(1)	—	—
Comprehensive loss	<u>\$ (7,975)</u>	<u>\$ (7,913)</u>	<u>\$ (1,865)</u>	<u>\$ (2,831)</u>
Reconciliation of net loss to net loss attributable to common stockholders				
Net loss	\$ (7,970)	\$ (7,912)	\$ (1,865)	\$ (2,831)
Accretion of redeemable convertible preferred stock to redemption value	(6,133)	(6,119)	(1,512)	(1,512)
Net loss attributable to common stockholders	<u>\$ (14,103)</u>	<u>\$ (14,031)</u>	<u>\$ (3,377)</u>	<u>\$ (4,343)</u>
Net loss per share attributable to common stockholders—basic and diluted(1)	<u>\$ (3.85)</u>	<u>\$ (3.76)</u>	<u>\$ (0.92)</u>	<u>\$ (1.14)</u>
Weighted-average number of common shares used in net loss per share attributable to common stockholders—basic and diluted(1)				
	<u>3,659,790</u>	<u>3,732,436</u>	<u>3,659,790</u>	<u>3,811,014</u>
Pro forma net loss per share attributable to common stockholders—basic and diluted (unaudited)(1)(2)		<u>\$ (0.10)</u>		<u>\$ (0.03)</u>
Pro forma weighted-average number of common shares used in net loss per share attributable to common stockholders—basic and diluted (unaudited)(1)(2)				
		<u>72,457,068</u>		<u>75,186,284</u>

	<u>As of December 31,</u>		<u>As of</u>
	<u>2012</u>	<u>2013</u>	<u>March 31,</u>
			<u>2014</u>
	<u>(in thousands)</u>		
<b>Balance Sheet Data:</b>			
Cash and cash equivalents	\$ 2,409	\$ 2,793	\$ 3,586
Working capital	6,499	(4,438)	(6,978)
Total assets	7,782	5,659	4,045
Preferred stock	90,286	96,405	97,917
Common stock and additional paid-in capital	4	4	4
Total stockholders' deficit	(86,656)	(100,514)	(104,840)

- (1) See Note 2 within the notes to our financial statements appearing elsewhere in this prospectus for a description of the method used to calculate basic and diluted net loss per common share and pro forma basic and diluted net loss per common share.
- (2) Pro forma to reflect the conversion of our preferred stock into shares of common stock upon the closing of this offering.

## MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

*You should read the following discussion and analysis of our financial condition and results of operations together with "Summary financial data," "Selected financial data" and our financial statements and related notes appearing elsewhere in this prospectus. Some of the information contained in this discussion and analysis or set forth elsewhere in this prospectus, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk Factors" section of this prospectus, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.*

### Overview

We are a late-stage biopharmaceutical company focused on the development of novel, first-in-class pharmaceuticals to address the needs of patients with renal and vascular disease. Our product candidate, PRT-201, is a recombinant human elastase that we are developing to reduce vascular access failure in patients with chronic kidney disease undergoing or preparing for hemodialysis, a lifesaving treatment that cannot be conducted without a functioning vascular access. We believe the data from our completed Phase 2 trial of PRT-201 in patients undergoing creation of an arteriovenous fistula, or AVF, support that a one-time, local application of PRT-201 during AVF surgical placement reduces AVF failure, thereby improving patient outcomes and reducing the burden on patients and the healthcare system. We are not aware of any approved preventative treatments to reduce the failure rate of AVFs. We expect to initiate the first of two Phase 3 trials for PRT-201 in radiocephalic AVFs, our initial indication, in the third quarter of 2014 and initiate the second Phase 3 trial in the first half of 2015.

We commenced business operations in June 2001. Our operations to date have been limited to organizing and staffing our company, business planning, raising capital, undertaking preclinical studies and clinical trials of PRT-201, protecting our intellectual property and providing general and administrative support for these operations. To date, we have not generated any product revenue and have primarily financed our operations through the private placement of our equity securities, business development activities, convertible note financings, and government grants. As of March 31, 2014, we had received an aggregate of \$87.3 million of net proceeds comprised of \$69.4 million from the issuance of equity securities, \$7.7 million from the issuance of convertible notes, \$10.0 million from business development activities and \$0.2 million from government grants. In addition, in May 2014, we received net proceeds of approximately \$24.7 million from the issuance of Series D convertible preferred stock to new and existing investors at a price per share of \$0.588656. In aggregate, 52,813,827 shares of Series D preferred stock were issued, including 10,344,201 shares for the conversion \$4.5 million of convertible notes and accrued interest at a conversion price of \$0.4414 per share.

As of March 31, 2014, we had an accumulated deficit of \$104.8 million. Our net losses were \$8.0 million and \$7.9 million for the years ended December 31, 2012 and 2013, respectively, and \$1.9 million and \$2.8 million, for the three months ended March 31, 2013 and 2014, respectively. We expect to incur significant expenses and increasing operating losses for the foreseeable future. We expect our research and development expenses to increase as we continue the clinical trials of, and seek regulatory approval for, PRT-201. If we obtain regulatory approval for PRT-201, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. Furthermore, following the closing of this offering, we expect that our general and administrative costs will increase as we grow and operate as a public company. As a result, we will need to generate significant revenue if we are to achieve profitability, and we may never be able to do so.

We believe that our available funds subsequent to this offering will be sufficient to fund our operations through \_\_\_\_\_, allowing us to obtain results from our first Phase 3 clinical trial of PRT-201 in \_\_\_\_\_.

radiocephalic AVFs and to accelerate the commencement of our second Phase 3 trial and the chemistry and manufacturing controls, or CMC, activities.

We do not expect to generate revenue from product sales unless and until we successfully complete development and obtain regulatory approval for PRT-201, which we expect will take a number of years and is subject to significant uncertainty. We have no manufacturing facilities and all of our manufacturing activities are contracted out to third parties. Additionally, we currently use third-party clinical research organizations, or CROs, to carry out our clinical development activities and we do not yet have a sales organization. If we obtain regulatory approval for PRT-201, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing, and distribution. Accordingly, we may seek to fund our operations through public or private equity or debt financings or other sources, including strategic collaborations. We may, however, be unable to raise additional funds or enter into such other arrangements when needed on favorable terms or at all. Our failure to raise capital or enter into such other arrangements as and when needed would have a negative impact on our financial condition and our ability to develop PRT-201 or any additional product candidates, if developed.

## **Financial Overview**

### ***Grant Revenue***

To date, our revenue has been derived solely from government grants. We did not receive any government grants during the reported periods and have no plans to receive additional government grants in the future.

### ***Research and Development Expenses***

Research and development expenses consist primarily of costs incurred for the development of PRT-201, which include:

- employee-related expenses, including salaries, benefits, travel and stock-based compensation expense;
- expenses incurred under agreements with CROs and investigative sites that will conduct our clinical trials;
- the cost of acquiring, developing, and manufacturing clinical trial materials;
- costs associated with regulatory operations; and
- facilities, depreciation, and other expenses, which include direct and allocated expenses for rent and maintenance of facilities, insurance, and other supplies.

We expense research and development costs to operations as incurred. We recognize costs for certain development activities, such as clinical trials, based on an evaluation of the progress to completion of specific tasks using data such as patient enrollment, clinical site activations or information provided to us by our vendors.

We cannot determine with certainty the duration and completion costs of the current or future clinical trials or if, when, or to what extent we will generate revenues from the commercialization and sale of PRT-201. We may never succeed in achieving regulatory approval for PRT-201. The duration, costs, and timing of clinical trials and development of PRT-201 will depend on a variety of factors, which include:

- the scope, rate of progress, and expense of our ongoing as well as any additional clinical trials and other research and development activities;
- uncertainties in clinical trial enrollment rate;
- future clinical trial results;
- significant and changing government regulation; and
- the timing and receipt of any regulatory approvals.



A change in any of these factors could mean a significant change in the costs and timing associated with the development of PRT-201. For example, if the FDA, or another regulatory authority were to require us to conduct clinical trials beyond those that we currently anticipate will be required for the completion of clinical development or if we experience significant delays in enrollment in any of our clinical trials, we could be required to expend significant additional financial resources and time on the completion of clinical development.

We expect our research and development expenses to increase for the foreseeable future as we continue the development of PRT-201. Our current planned development activities include the following:

- we plan to commence our first Phase 3 clinical trial of PRT-201 for patients undergoing creation of a radiocephalic AVF in the third quarter of 2014. Prior to completing enrollment in the first Phase 3 trial, we intend to initiate our second Phase 3 trial. If the results from the first Phase 3 trial are sufficiently compelling, we intend to meet with the FDA to discuss the possibility of submitting a BLA, supported by the single Phase 3 trial and may decide to submit a BLA to the FDA prior to completing the second Phase 3 trial;
- we may, based on additional data including the data from our Phase 3 clinical trials and if sufficient funds become available, choose to conduct a clinical trial of PRT-201 in Europe;
- we may, based on additional data including the data from our Phase 3 clinical trials and if sufficient funds become available, study the effects of a 30 microgram dose of PRT-201 versus placebo on brachiocephalic AVFs and in patients undergoing placement of an arteriovenous graft, or AVG; and
- we expect to continue to manufacture clinical trial materials in support of our clinical trials.

Our direct research and development expenses consist principally of external costs, such as fees paid to CROs, investigators, consultants and central laboratories in connection with our clinical trials, and costs related to acquiring and manufacturing clinical trial materials as well as of salaries and related costs for personnel, including stock-based compensation and travel expenses.

#### ***General and Administrative Expenses***

General and administrative expenses consist principally of salaries and related costs for personnel, including stock-based compensation and travel expenses, in executive and other administrative functions. Other general and administrative expenses also include professional fees for legal, patent review, consulting and accounting services as well as facility related costs. We anticipate increased expenses related to audit, legal, regulatory, and tax-related services associated with maintaining compliance with our NASDAQ listing and Securities and Exchange Commission requirements, director and officer insurance premiums, and investor relations costs associated with being a public company.

Additionally, if and when we believe a regulatory approval of our first product candidate appears likely, we anticipate that we will increase our salary and personnel costs and other expenses as a result of our preparation for commercial operations.

#### ***Interest Expense, Net***

Interest expense, net, consists of interest incurred on debt instruments, amortized deferred financing costs and amortized debt discount, as offset by any interest income earned on our cash, cash equivalents and marketable securities. The debt discount primarily consists of the fair value of the bifurcated features embedded in the convertible notes issued in September 2013. As of March 31, 2014, the debt discount had been fully amortized to interest expense.

#### ***Other Income (Expense)***

Other income consists of the gain realized by the sale of fixed assets as well as changes in fair market value of the derivative liability associated with the convertible notes.

### ***Accretion of Preferred Stock***

Subsequent to the May 2014 Series D convertible preferred stock financing, our shares of preferred stock are redeemable beginning in 2019 at their original issuance price plus any declared or accrued but unpaid dividends upon written election of the preferred stockholders in accordance with the terms of our certificate of incorporation. Accretion of preferred stock reflects the accretion of issuance costs and cumulative dividends on our preferred stock based on their respective redemption values.

### **Critical Accounting Policies and Significant Judgments and Estimates**

Our management's discussion and analysis of our financial position and results of operations is based on our financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles, or GAAP. The preparation of financial statements in conformity with GAAP requires us to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. On an ongoing basis, we evaluate estimates, which include estimates related to clinical trial accruals, stock-based compensation expense, embedded derivatives, and reported amounts of revenues and expenses during the reported period. We base our estimates on historical experience and other market-specific or other relevant assumptions that we believe to be reasonable under the circumstances. Actual results may differ materially from those estimates or assumptions.

While our significant accounting policies are described in more detail in the notes to our financial statements appearing elsewhere in this prospectus, we believe the following accounting policies to be most critical to the judgments and estimates used in the preparation of our financial statements.

#### ***Accrued Research and Development Expenses***

As part of the process of preparing our financial statements, we are required to estimate our accrued expenses. This process involves reviewing open contracts and purchase orders, communicating with our personnel to identify services that have been performed for us and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. The majority of our service providers invoice us monthly in arrears for services performed or when contractual milestones are met. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. Examples of estimated accrued research and development expenses include fees paid to CROs in connection with clinical trials and vendors related to manufacturing, development and distribution of clinical supplies.

We base our expenses related to clinical trials on our estimates of the services received and efforts expended pursuant to contracts with multiple CROs that conduct and manage clinical trials on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the clinical expense. Payments under some of these contracts depend on factors such as the successful enrollment of subjects and the completion of clinical trial milestones. In accruing service fees, we estimate the time period over which services will be performed, enrollment of subjects, number of sites activated and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepaid accordingly. Although we do not expect our estimates to be materially different from amounts actually incurred, if our estimates of the status and timing of services performed differs from the actual status and timing of services performed we may report amounts that are too high or too low in any particular period. To date, there have been no material differences from our estimates to the amount actually incurred.

### ***Derivative Instruments***

We occasionally issue financial instruments in which a derivative instrument is "embedded." Upon issuing the financial instrument, we assesses whether the economic characteristics of the embedded derivative are clearly and closely related to the economic characteristics of the remaining component of the financial instrument (*i.e.*, the host contract) and whether a separate, non-embedded instrument with the same terms as the embedded instrument would meet the definition of a derivative instrument as defined in ASC 815 *Derivatives and Hedging*. When it is determined that (1) the embedded derivative possesses economic characteristics that are not clearly and closely related to the economic characteristics of the host contract and (2) a separate, stand-alone instrument with the same terms would qualify as a derivative instrument, the embedded derivative is separated from the host contract and carried at fair value with changes in fair value recorded in current period earnings.

### ***Convertible Notes***

On September 4, 2013, we issued, at par value, convertible promissory notes with an aggregate principal amount of approximately \$4.3 million. The notes were due March 31, 2014, upon written notice from holders of a majority of the then-outstanding aggregate principal amount, and accrued interest at an annual rate of 8%. We determined that the debt contained certain features requiring evaluation for separate accounting from the fixed interest rate host instrument including (i) holder's optional conversion upon maturity; (ii) mandatory conversion upon a reverse acquisition; (iii) automatic conversion upon a qualified financing; (iv) holder's optional conversion upon a non-qualified financing; (v) issuer's optional redemption; (vi) redemption upon a change in control; (vii) put upon a breach; and (viii) a put upon an event of default. In certain cases these features require us to either convert the notes or accelerate their repayment at a significant premium to the principal and accrued interest then outstanding.

The embedded features requiring separate accounting were combined and valued upon issuance using a single income valuation approach. As of September 4, 2013, December 31, 2013, and March 31, 2014, we ascribed a probability to the automatic conversion upon a qualified financing of 85%, 100% and 100%, respectively. As of September 4, 2013, December 31, 2013, and March 31, 2014, we ascribed a probability to the redemption feature upon a change in control of 15%, 0% and 0%, respectively. For all other features included in the combined embedded derivative, we estimated a 0% probability of occurrence at all times.

We recorded approximately \$1.4 million as the fair value of the combined embedded derivative liability on September 4, 2013, with a corresponding amount recorded as debt discount. The debt discount has been amortized to interest expense over the life of the notes using the effective interest method. As of December 31, 2013 and March 31, 2014, the fair value of the combined embedded derivative liability was \$1.4 million and \$1.5 million, respectively. Changes in the estimated fair value of the embedded features were recorded in earnings in the period in which they occurred.

In connection with the issuance of our Series D convertible preferred stock on May 13, 2014, the notes in the aggregate amount of approximately \$4.5 million in principal plus accrued interest were converted into 10,344,201 shares of Series D convertible preferred stock. As the debt discount had been fully amortized prior to conversion, there was no gain or loss recognized upon conversion of the notes.

### ***Stock-Based Compensation***

From our inception in June 2001, until December 31, 2005, we applied the guidance in Accounting Principles Bulletin, or APB 25. Under APB 25, there is no stock-based compensation expense recognized for awards granted with an exercise price equal to the fair value of the underlying stock on the date of grant.

Since January 1, 2006, we have applied the fair value recognition provisions of Financial Accounting Standards Board, or FASB, Accounting Standards Codification or ASC, Topic 718, *Compensation—Stock Compensation*, or ASC 718, to account for stock-based compensation for employees. ASC 718 applies to any awards granted, modified, repurchased, or canceled after December 31, 2005, and requires the measurement and recognition of costs for all stock-based awards made to employees and directors, including stock options, stock appreciation rights, stock units, and discounted employee stock purchases. We recognize compensation costs related to employees based on the estimated fair value of the awards on the date of grant and over the requisite service periods, using the straight-line method. The options vest periodically over various schedules and all options expire no later than ten years after the date of grant.

We have applied the fair value recognition provisions of ASC 718 and FASB ASC 505, *Equity*, to account for stock-based compensation for non-employees. Stock-based compensation related to non-employee awards is re-measured at each reporting period until the awards are vested and is estimated using an expected term equal to the remaining contractual term of the award. Compensation expense is recognized for the fair value of the consideration received, or the equity instruments issued, whichever is more reliably measurable. We recorded compensation expense for non-employee awards with graded vesting using the accelerated expense attribution method.

We estimate the fair value of our stock-based awards to employees and non-employees using the Black-Scholes option pricing model, which requires the input of highly subjective assumptions, including: (1) the expected volatility of our stock, (2) the expected term of the award, (3) the risk-free interest rate and (4) expected dividends. Due to the lack of a public market for the trading of our common stock and a lack of company specific historical and implied volatility data, we have based our estimate of expected volatility on the historical volatility of a group of comparable companies that are publicly traded. For these analyses, we selected representative companies from the life sciences industry with characteristics similar to ours, including enterprise value, risk profiles, position within the industry and historical share price information, sufficient to meet the expected life of the stock-based awards. We compute the historical volatility data using the daily closing prices for the selected companies' shares during the equivalent period of the calculated expected term of our stock-based awards. We will continue to apply this process until a sufficient amount of historical information regarding the volatility of our own stock price becomes available. We use a dividend yield of zero based on the fact that we have never declared cash dividends and have no current intention of paying cash dividends over the expected term of the option. As we do not have sufficient historical stock option activity data to provide a reasonable basis upon which to estimate the expected term of stock options granted to employees, we have estimated the expected life of our employee stock options using the "simplified" method, whereby the expected life equals the average of the vesting term and the original contractual term of the option. For non-employee options, we have determined the expected life based on the respective contractual life. The risk-free interest rates for periods within the expected life of the option are based on the U.S. Treasury yield curve in effect during the period the options were granted and with maturity dates equivalent to the expected term of the option.

The following table presents the grant dates of shares subject to awards from January 1, 2012 through June 24, 2014 along with the corresponding exercise price for each option grant and our current estimate of the fair value per share of our common stock on each grant date, which we utilize to calculate stock-based compensation expense:

<u>Date of Grant</u>	<u>Number of Underlying Options Granted</u>	<u>Exercise Price per Share</u>	<u>Current Estimate of Common Stock Fair Value per Share on Grant Date</u>
3/25/2013	50,000	\$ 1.40	\$ 1.40
6/24/2014	8,375,000	\$ 0.31	\$ 0.31

*Determination of the Fair Value of Common Stock on Grant Dates*

Following the consummation of this offering, the fair value of our common stock will be determined based on the quoted market price of our common stock. We have historically granted stock options at exercise prices not less than the fair value of our common stock. Our board of directors determined the fair value of our common stock considering, in part, the work of an independent third-party valuation specialist. The board determined the estimated per share fair value of our common stock at various dates considering contemporaneous valuations performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants Practice Aid, *Valuation of Privately-Held Company Equity Securities Issued as Compensation*, also known as the "Practice Aid".

In conducting the valuations, the independent third-party valuation specialist considered all objective and subjective factors that it believed to be relevant for each valuation conducted in accordance with the Practice Aid, including our best estimate of our business condition, prospects and operating performance at each valuation date. Other significant factors included:

- the prices of our preferred stock sold to outside investors in arm's length transactions, and the rights, preferences and privileges of our preferred stock as compared to those of our common stock, including the liquidation preferences of our preferred stock;
- the provisions of an option agreement to acquire Proteon that has since terminated;
- our results of operations, financial position and the status of research and development efforts;
- the composition of, and changes to, our management team and board of directors;
- the lack of liquidity of our common stock;
- our stage of development and business strategy and the material risks related to our business and industry;
- the valuation of publicly traded companies in the life sciences sector, as well as recently completed mergers and acquisitions of guideline companies;
- any external market conditions affecting the life sciences industry sector; and
- the likelihood of achieving a liquidity event for the holders of our common stock and stock options, such as an initial public offering, or IPO, or a sale of our company, given prevailing market conditions, and the state of the IPO market for similarly situated privately held life sciences companies.

The dates of our contemporaneous and retrospective valuations have not always coincided with the dates of our stock option grants. In determining the exercise prices of the stock options set forth in the table above, our board of directors considered, among other things, the most recent contemporaneous and retrospective valuation of our common stock and their assessment of additional objective and subjective factors that were relevant as of the grant dates. The additional factors considered when determining whether any changes in the fair value of our common stock had occurred between the most recent contemporaneous valuation and the grant dates included our stage of research and development, our operating and financial performance and current business conditions.

There are significant judgments and estimates inherent in the determination of the fair value of our common stock. These judgments and estimates include assumptions regarding our future operating performance, the time to completing an IPO or other liquidity event, the related valuations associated with these events, and the determinations of the appropriate valuation methods at each valuation date. If we had made different assumptions, our stock-based compensation expense, net loss and net loss per share applicable to common stockholders could have been materially different.

*Common Stock Valuation Methodologies*

The valuations we obtained were prepared in accordance with the guidelines in the Practice Aid, which prescribes several valuation approaches for setting the value of an enterprise, such as the cost, market and income approaches, and various methodologies for allocating the value of an enterprise to its

common stock. We generally used the market approach, in particular the guideline public company and guideline transaction methodologies, based on inputs from comparable public companies' equity valuations and comparable acquisition transactions, to estimate the enterprise value of our company.

#### *Methods Used to Allocate Our Enterprise Value to Classes of Securities*

In accordance with the Practice Aid, we considered the various methods for allocating the enterprise value across our classes and series of capital stock to determine the fair value of our common stock at each valuation date. The methods and scenarios considered consisted of the following:

- *Probability-Weighted Expected Return Method, or PWERM.* The PWERM is a scenario-based analysis that estimates the value per share based on the probability-weighted present value of expected future investment returns, considering each of the possible outcomes available to us, as well as the economic and control rights of each share class. Our PWERM analyses assume a range of exit scenarios, including an IPO, and allocate the value in each scenario according to our capital structure, probability-weighting each exit and discounting the value to a present value equivalent using a risk-adjusted discount rate.
- *Option Pricing Method, or OPM.* Under the option pricing method, shares are valued by creating a series of call options with exercise prices based on the liquidation preferences and conversion terms of each equity class. The values of the preferred and common stock are inferred by analyzing these options. Our OPM analysis evaluates a scenario where we remain private and is modeled over a weighted average term to exit using a recent financing round as the basis for fair market value determination.
- *Hybrid Method.* The hybrid method employs the concepts of the PWERM and OPM merged into a single framework.

The foregoing valuation methodologies are not the only methodologies available and they will not be used to value our common stock once this offering is complete. We cannot make assurances as to any particular valuation for our common stock. Accordingly, investors are cautioned not to place undue reliance on the foregoing valuation methodologies as an indicator of future stock prices.

## **Results of Operations**

### *Comparison of the Three Months Ended March 31, 2013 and March 31, 2014*

	<b>Three Months Ended</b>		<b>Period-to- Period Change</b>
	<b>March 31,</b>		
	<b>2013</b>	<b>2014</b>	
	<b>(in thousands)</b>		
Operating expenses:			
Research and development	\$ 1,134	\$ 1,189	\$ 55
General and administrative	737	744	7
Total operating expenses	<u>1,871</u>	<u>1,933</u>	<u>62</u>
Loss from operations	<u>(1,871)</u>	<u>(1,933)</u>	<u>(62)</u>
Other income (expense):			
Interest expense	2	(828)	(830)
Other income (expense)	4	(70)	(74)
Total other income (expense)	<u>6</u>	<u>(898)</u>	<u>(904)</u>
Net loss	<u>\$ (1,865)</u>	<u>\$ (2,831)</u>	<u>\$ (966)</u>

*Research and Development Expenses.* The following table identifies research and development expenses on both an external and internal basis for the three months ended March 31, 2013 and 2014:

	Three Months Ended March 31,		Period-to- Period Change
	2013	2014	
	(in thousands)		
External research and development expenses	\$ 579	\$ 678	\$ 99
Internal research and development expenses	555	511	\$ (44)
Total research and development expenses	<u>\$ 1,134</u>	<u>\$ 1,189</u>	<u>\$ 55</u>

During the three months ended March 31, 2014, our total research and development expenses increased by \$0.1 million compared to the three months ended March 31, 2013, primarily due to increased manufacturing, process development and quality assurance expenses related to our upcoming radiocephalic AVF Phase 3 clinical trials. Our external research and development spending increased by \$0.1 million primarily due to this increase in manufacturing, process development and quality assurance expenses in preparation for the radiocephalic AVF Phase 3 trials offset by a decrease in clinical trial spending. Our internal research and development expenses decreased by \$44,000 in the three months ended March 31, 2014 compared to the three months ended March 31, 2013, primarily due to a nonrecurring charge for stock-based compensation expense in the three months ended March 31, 2013 arising from the modification of an employee's stock option award.

*General and Administrative Expenses.* During the three months ended March 31, 2014, our total general and administrative expenses were essentially the same as compared to the three months ended March 31, 2013. Changes from the prior period included additional overhead and personnel costs in the three months ended March 31, 2014 of \$0.1 million to support our on-going corporate activities offset by a decrease of \$0.1 million in legal expenses for our patents.

*Other Expense.* During the three months ended March 31, 2014, other expenses increased by \$0.1 million related to the change in fair market value of the derivative liability associated with the convertible promissory notes.

*Interest Expense, Net.* During the three months ended March 31, 2014, interest expense, net increased by \$0.8 million due to the interest expense on our convertible promissory notes.

#### **Comparison of the Years Ended December 31, 2012 and December 31, 2013**

	Years Ended December 31,		Period-to- Period Change
	2012	2013	
	(in thousands)		
Operating expenses:			
Research and development	\$ 5,907	\$ 3,994	\$ (1,913)
General and administrative	2,089	3,128	1,039
Total operating expenses	<u>7,996</u>	<u>7,122</u>	<u>(874)</u>
Loss from operations	<u>(7,996)</u>	<u>(7,122)</u>	<u>874</u>
Other income (expense):			
Interest expense	20	(857)	(877)
Other income	6	67	61
Total other income (expense)	<u>26</u>	<u>(790)</u>	<u>(816)</u>
Net loss	<u>\$ (7,970)</u>	<u>\$ (7,912)</u>	<u>\$ 58</u>

*Research and Development Expenses.* The following table identifies research and development expenses on both an external and internal basis for the years ended December 31, 2012 and 2013:

	Years Ended December 31,		Period-to- Period Change
	2012	2013	
		(in thousands)	
External research and development expenses	\$ 3,514	\$ 1,962	\$ (1,552)
Internal research and development expenses	2,393	2,032	(361)
Total research and development expenses	<u>\$ 5,907</u>	<u>\$ 3,994</u>	<u>\$ (1,913)</u>

During the year ended December 31, 2013, our total research and development expenses decreased by \$1.9 million compared to the prior year, primarily due to the completion of our AVF Phase 2 trial and our AVG Phase 1/2 trial. Our external research and development expenses decreased by \$1.5 million primarily due to a reduction in expenses related to our clinical trials and our manufacturing and process development. Our internal research and development expenses decreased by \$0.4 million primarily due to a reduction in our research and development employees and contractors.

*General and Administrative Expenses.* During the year ended December 31, 2013, our total general and administrative expenses increased by \$1.0 million compared to the prior year. This increase was primarily due to additional overhead and personnel costs in 2013 of \$0.5 million to support our ongoing corporate activities and \$0.5 million related to higher legal expenses.

*Other Income (Expense).* During the year ended December 31, 2013, our other income increased by \$0.1 million due to a gain from the sale of fixed assets.

*Interest Expense, Net.* During the year ended December 31, 2013, our interest expense, net increased by \$0.8 million due to the interest expense on our convertible promissory notes.

## Liquidity and Capital Resources

### Overview

Since our inception and through March 31, 2014, we had received \$87.3 million in net proceeds million comprised of \$69.4 million from the issuance of equity securities, \$7.7 million from the issuance of convertible notes, \$10.0 million from business development activities and \$0.2 million from government grants. At March 31, 2014, our cash and cash equivalents were \$3.6 million.

### Convertible Note Financings

In April 2013, we entered into a convertible note purchase agreement with some of our existing preferred stockholders whereby we had the option, but not the obligation, to issue convertible promissory notes in the aggregate principal amount of approximately \$4.3 million, subject to meeting at least one of two pre-determined conditions. In September 2013, upon satisfying one of the conditions, we issued the notes, which accrue interest at 8% annum and mature on or after March 31, 2014 upon written notice from a majority of the outstanding note holders.

As further described above and within our financial statements appearing elsewhere in this prospectus, in connection with the issuance of the convertible notes, we recorded \$1.4 million as a discount on the convertible notes related to the estimated fair value of the combined embedded derivative liability and certain issuance costs. The discount was amortized to interest expense over the life of the convertible notes. Changes in the estimated fair value of the combined embedded derivative liability were recorded in earnings in the periods in which they occurred.



On May 13, 2014, upon the closing of our Series D convertible preferred stock financing described below, the convertible notes, in the aggregate amount of approximately \$4.5 million principal and accrued interest automatically converted into 10,344,201 shares of our Series D convertible preferred stock at a conversion price per share of \$0.4414.

### ***Series D Financing***

On May 13, 2014, we received net proceeds of approximately \$24.7 million from the issuance of Series D convertible preferred stock to new and existing investors at a price per share of \$0.588656. In aggregate, we issued 52,813,827 shares of Series D preferred stock including 10,344,201 shares for the conversion of \$4.5 million of convertible notes and accrued interest at a conversion price of \$0.4414 per share. As provided by the Series D stock purchase agreement, the investors in the Series D convertible preferred stock have the potential opportunity to invest an additional \$20.0 million in Series D convertible preferred stock at \$0.588656 per share. The investors' rights to purchase additional shares of Series D preferred stock will terminate with this offering.

### ***Operating Capital Requirements***

We expect to incur increasing operating losses for at least the next several years as we conduct our Phase 3 clinical trials for PRT-201 in radiocephalic AVFs, thereafter seeking marketing approval for PRT-201 in radiocephalic AVFs assuming successful trial outcomes, and pursue development of PRT-201 for additional indications, including in brachiocephalic AVFs and AVGs. We may not be able to complete the development and initiate commercialization of PRT-201 if, among other things, our clinical trials are not successful, the Food and Drug Administration does not approve PRT-201 when we expect, or at all.

We believe that the net proceeds of this offering, together with our existing cash and cash equivalents, will be sufficient to fund our operations through . Based on our planned use of the net proceeds of this offering and our existing cash resources, we believe that our available funds subsequent to this offering will be sufficient to enable us to obtain results from our first Phase 3 clinical trial of PRT-201 in radiocephalic AVFs and to accelerate the commencement of our second Phase 3 trial and the chemistry and manufacturing controls, or CMC, activities.

Unless or until we can generate a sufficient amount of revenue from our product sales we expect to fund our operations through a combination of equity offerings debt financings or other sources including potential collaborations. Additional capital may not be available on favorable terms, if at all. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of one or more of our protein therapeutic candidates. If we raise additional funds through the issuance of debt or equity securities, it could result in dilution to our existing stockholders and increased fixed payment obligations, and these securities may have rights senior to those of our common stock. If we incur indebtedness, we could become subject to covenants that would restrict our operations and potentially impair our competitiveness, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. We may not be able to enter into collaboration arrangements for PRT-201 in targeted geographies. Any of these events could significantly harm our business, financial condition and prospects.

Our forecast of the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement and involves risks and uncertainties, and actual results could vary as a result of a number of factors. We have based this estimate on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we currently expect. Our future funding requirements, both near and long-term, will depend on many factors, including:

- the timing and costs of our planned Phase 3 clinical trials of PRT-201 in radiocephalic AVFs;

- the timing and costs of developing PRT-201 for additional indications;
- the outcome, timing and costs of seeking regulatory approvals;
- the costs of commercialization activities for PRT-201 in radiocephalic AVFs and other indications if we receive marketing approval, including the costs and timing of establishing product sales, marketing, distribution and manufacturing capabilities;
- subject to receipt of marketing approval, revenue received from commercial sales of PRT-201;
- the terms and timing of any future collaborations, licensing, consulting or other arrangements that we may establish;
- the amount and timing of any payments we may be required to make, or that we may receive, in connection with the licensing, filing, prosecution, defense and enforcement of any patents or other intellectual property rights, including royalty payments that we are obligated to pay to Johns Hopkins University pursuant to our assignment agreement related to PRT-201;
- the costs of preparing, filing and prosecuting patent applications, maintaining and protecting our intellectual property rights and defending against intellectual property related claims; and
- the extent to which we in-license or acquire other products and technologies.

### **Cash Flows**

The following table summarizes our sources and uses of cash:

	Years Ended December 31,		Three Months Ended March 31,	
	2012	2013	2013	2014
	(in thousands)			
Net cash used in operating activities	\$ (8,234)	\$ (6,657)	\$ (1,788)	\$ (1,562)
Net cash provided by investing activities	7,382	2,727	1,794	2,355
Net cash (used in) provided by financing activities	(9)	4,314	—	0
Net (decrease) increase in cash and cash equivalents	\$ (861)	\$ 384	\$ 6	\$ 793

### **Comparison of the Three Months Ended March 31, 2013 and 2014**

Net cash used in operating activities was \$1.8 million during the three months ended March 31, 2013 compared to \$1.6 million during the three months ended March 31, 2014. The decrease of \$0.2 million in cash used in operating activities in the first three months of 2014 was primarily driven by an increase in our operating expenses of \$0.1 million offset by a decrease in working capital balances and an increase in non-cash operating expenses of \$0.3 million as compared to the first three months of 2013.

Net cash provided by investing activities was \$1.8 million during the three months ended March 31, 2013 compared to \$2.4 million during the three months ended March 31, 2014. The increase in cash provided by investing activities of \$0.6 million in the first three months of 2014 was driven by a decrease in the purchases of available for sale investments of \$1.5 million offset by a decrease in maturities of short term investments of \$0.9 million compared to the first three months of 2013, as all short term investments held in the first three months of 2014 matured and there were no new purchases during the period.

Net cash provided by financing activities during the three months ended March 31, 2013 and March 31, 2014 was immaterial.

### **Comparison of the Years Ended December 31, 2012 and 2013**

Net cash used in operating activities was \$8.2 million for the year ended December 31, 2012 compared to \$6.7 million for the year ended December 31, 2013. The decrease of \$1.6 million in cash used in operating activities was primarily driven by a \$0.9 million decrease in our operating expenses and the

\$0.7 million increase in the non-cash adjustment for the accretion of the debt discount and the debt issuance cost provided by convertible notes payable.

Net cash provided by investing activities was \$7.4 million for the year ended December 31, 2012 compared to net cash provided of \$2.7 million for the year ended December 31, 2013. The decrease of \$4.7 million in cash provided by investing activities was driven by a decrease in net proceeds from maturities of available for sale short term investments of \$9.5 million offset by a decrease in purchases of available for sale short term investments of \$4.8 million compared to the prior year.

Net cash provided by financing activities during the year ended December 31, 2012 was immaterial. Net cash provided by financing activities during the year ended December 31, 2013 of approximately \$4.3 million was attributable to our September 2013 convertible promissory note financing.

#### **Off-Balance Sheet Arrangements**

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined under the applicable regulations of the Securities Exchange Commission, or SEC.

#### **Net Operating Loss Carryforwards**

As of December 31, 2013, we had federal and state net operating loss carryforwards of approximately \$69.9 million and \$45.4 million, respectively, to offset future federal and state taxable income, which will expire at various times between 2014 and 2033. We also had federal and state research and development tax credit carryforwards of approximately \$2.0 million and \$1.1 million, respectively, to offset future income taxes, which will expire at various times between 2022 and 2033. Lastly, as of December 31, 2013, we had federal Orphan Drug tax credit carryforwards of approximately \$7.2 million, to offset future income taxes, which will expire at various times between 2029 and 2033. Net operating loss and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service and state tax authorities and may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant stockholders over a three-year period in excess of 50%, as defined under Sections 382 and 383 of the United States Internal Revenue Code of 1986, as amended, as well as similar state provisions. This could limit the amount of tax attributes that can be utilized annually to offset future taxable income or tax liabilities. The amount of the annual limitation is determined based on the value of our company immediately prior to the ownership change. Subsequent ownership changes may further affect the limitation in future years. On December 31, 2013, we recorded a 100% valuation allowance against our net operating loss and tax credit carryforwards, as we believe it is more likely than not that the tax benefits will not be fully realized. In the future, if we determine that a portion or all of the tax benefits associated with our tax carryforwards will be realized, net income would increase in the period of such determination.

**Contractual Obligations**

The following table summarizes our outstanding contractual obligations as of payment due date by period at December 31, 2013:

	Total	Less than 1 Year	1 to 3 Years (in thousands)	3 to 5 Years	More than 5 Years
Convertible promissory notes(1)	\$ 4,452	\$ 4,452	\$ —	\$ —	\$ —
Operating leases(2)	188	188	—	—	—
<b>Total obligations</b>	<b>\$ 4,640</b>	<b>\$ 4,640</b>	<b>\$ —</b>	<b>\$ —</b>	<b>\$ —</b>

- (1) The convertible promissory notes represent the aggregate \$4.3 million principal amount of convertible notes issued in September of 2013 plus accrued interest totaling \$0.1 million. The convertible notes were converted into Series D preferred stock in May 2014.
- (2) In July 2009 we entered into a multi-year non-cancelable lease for our offices in Waltham, Massachusetts. In October 2011, we amended the lease extending its expiration to December 2014. The minimum lease payments above do not include common area maintenance charges or real estate taxes.

The contractual obligations table does not include any potential future royalty payments we may be required to make under our license assignment with Johns Hopkins University, due to the uncertainty of the occurrence of the events requiring payment under that agreement.

We enter into contracts in the normal course of business with CROs and clinical sites for the conduct of clinical trials, professional consultants for expert advice and other vendors for clinical supply manufacturing or other services. These contracts are not included in the table above as they provide for termination on notice, and therefore are cancelable contracts and do not include any minimum purchase commitments.

**Qualitative and Quantitative Disclosures about Market Risk**

The market risk inherent in our financial instruments and in our financial position represents the potential loss arising from adverse changes in interest rates. As of March 31, 2014, we had cash equivalents of \$3.6 million consisting primarily of investments in U.S. Treasuries and certificates of deposit. Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our investments are in short-term marketable securities. Our marketable securities are subject to interest rate risk and could fall in value if market interest rates increase. Due to the short-term duration of our investment portfolio and the low risk profile of our investments, an immediate 10% change in interest rates would not have a material effect on the fair market value of our investment portfolio. We have the ability to hold our marketable securities until maturity, and therefore we would not expect our operating results or cash flows to be affected to any significant degree by the effect of a change in market interest rates on our investments.

We contract with CROs and contract manufacturers internationally. Transactions with these providers are predominantly settled in U.S. dollars and, therefore, we believe that we have only minimal exposure to foreign currency exchange risks. We do not hedge against foreign currency risks.

**The JOBS Act**

In April 2012, the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, was enacted. Section 107 of the JOBS Act provides that an "emerging growth company," or EGC, can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act of 1933, as amended, or the Securities Act, for complying with new or revised accounting standards. As a result, an EGC can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this extended transition period and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies.

## BUSINESS

### Overview

We are a late-stage biopharmaceutical company focused on the development of novel, first-in-class pharmaceuticals to address the needs of patients with renal and vascular disease. Our product candidate, PRT-201, is a recombinant human elastase that we are developing to reduce vascular access failure in patients with chronic kidney disease undergoing or planning for hemodialysis, a lifesaving treatment that cannot be conducted without a functioning vascular access. We believe the data from our completed Phase 2 trial of PRT-201 in patients undergoing creation of an arteriovenous fistula, or AVF, support that a one-time, local application of PRT-201 during AVF surgical placement reduces AVF failure, thereby improving patient outcomes and reducing the burden on patients and the healthcare system. We are not aware of any approved preventative treatments to reduce the failure rate of AVFs. We expect to initiate the first of two Phase 3 trials for PRT-201 in radiocephalic AVFs, our initial indication, in the third quarter of 2014 and initiate the second Phase 3 trial in the first half of 2015.

The need to improve vascular access outcomes is well established in the hemodialysis community. A 2014 publication estimated the total cost of managing hemodialysis vascular access dysfunction in the United States to be approximately \$2.9 billion annually. AVFs are the gold standard of vascular access for hemodialysis, given they are associated with fewer complications and reduced rates of hospitalization than other forms of vascular access. We estimate there are approximately 130,000 AVFs created in the United States annually, a procedure in which a surgeon transects a vein and sutures it to the side of a nearby artery, typically in the arm. However AVFs have a greater than 50% failure rate in their first year after placement, resulting in frequent surgical or interventional procedures and a high rate of abandonment, leading to increased morbidity, mortality and costs of care. Function can usually be restored via additional procedures, either an intervention such as angioplasty, which is dilation of a blood vessel with a balloon, or a surgical revision. However, these procedures are costly, invasive, painful, associated with a number of complications and often need to be repeated. AVF patients in the United States on average require greater than 1.5 procedures per year, each of which typically costs Medicare between \$5,000 and \$13,000.

We demonstrated that PRT-201 generates fragments of elastin, a protein present in blood vessels, and we believe the fragments of elastin inhibit formation of neointimal hyperplasia, which is the growth of tissue inside vessels that narrows AVFs and reduces blood flow. We believe that a one-time, local application of PRT-201 to the external surface of the vessels during AVF surgical placement can modify the injury response, or scarring, resulting from surgery and thereby reduce the severity of neointimal hyperplasia and AVF failure following surgery.

We have completed a multicenter, randomized double-blind, placebo-controlled Phase 2 trial of PRT-201 in 151 patients undergoing surgical creation of AVFs in the wrist, known as radiocephalic AVF, or upper arm, known as brachiocephalic AVF. The primary efficacy endpoint was primary unassisted patency, defined as the time from surgical creation of the AVF to occurrence of a thrombosis or an intervention such as angioplasty, to restore or maintain patency, or functionality. Both the 10 microgram and 30 microgram doses of PRT-201 showed a trend toward efficacy on the primary endpoint, although neither dose met the primary endpoint with statistical significance. For all AVFs, median patency, the time at which 50% of patients in a group lost primary unassisted patency, was 224 days in the placebo group and greater than 365 days in each of the PRT-201 treatment groups, indicating that PRT-201 prolonged primary unassisted patency. In the trial, patients treated with PRT-201 reported adverse events comparable to placebo. These events were consistent with the medical events experienced by chronic kidney disease patients undergoing AVF placement surgery.

An analysis of the primary endpoint data revealed an uneven distribution in patency loss events due to central stenosis in the shoulder and chest, remote from the site of an AVF. Central stenoses commonly exist prior to surgery and are unrelated to treatment with PRT-201. Therefore, to correct for this uneven distribution, we conducted a non-prespecified analysis of the primary endpoint that excluded patency loss

events due to central stenoses. This analysis demonstrated a significant reduction in the risk of primary unassisted patency loss in the 30 microgram PRT-201 dose group (p=0.04) compared to placebo.

The benefit of PRT-201 on primary unassisted patency was most pronounced in the subset of patients undergoing placement of a radiocephalic AVF. The subset analysis of this endpoint for radiocephalic AVF patients receiving the 30 microgram dose, which was not prespecified, showed a significant increase in median primary unassisted patency of >365 days as compared to 125 days in the placebo group. In addition, we observed beneficial drug effects on additional efficacy endpoints, including unassisted maturation, defined as increased vessel diameter and blood flow without the need for an intervention such as angioplasty; rate of procedures to restore or maintain AVF patency; secondary patency, defined as abandonment of the AVF and the need for creation of a new vascular access; use for hemodialysis and hemodynamically significant stenosis, or narrowing of blood vessels.

In April 2013, we held an end of Phase 2 meeting with the United States Food and Drug Administration, or FDA, during which we confirmed elements of our Phase 3 development plan, including the primary endpoint. We plan to perform two 300-patient Phase 3 trials of PRT-201 using a 30 microgram dose, which will enroll patients undergoing a surgical procedure to create a radiocephalic AVF. We plan to begin enrolling patients in our first Phase 3 clinical trial in the third quarter of 2014, and anticipate that results will be available in 2017. We expect to initiate our second Phase 3 clinical trial in the first half of 2015. In May 2014, following the results from our Phase 2 trial and to fund our first Phase 3 trial, we closed on the \$25.0 million first tranche of a \$45.0 million total financing. The financing was led by Abingworth, Deerfield and Pharmstandard and included investments from our existing venture investors. If the results of the first Phase 3 trial are sufficiently compelling, we intend to meet with the FDA to discuss the possibility of submitting a Biologics License Application, or BLA, supported by the single Phase 3 trial and may decide to submit a BLA to the FDA prior to completing the second Phase 3 trial. PRT-201 has received fast track designation from the FDA and orphan drug designation in the United States and European Union, for hemodialysis vascular access indications.

We believe that if our Phase 3 clinical program is successful PRT-201 will potentially become the standard of care for patients with chronic kidney disease who are undergoing surgical placement of a radiocephalic AVF. We retain worldwide commercial rights to PRT-201. If approved by regulatory authorities, we intend to commercialize this product in the United States ourselves with a specialty hospital sales force, focused primarily on vascular surgeons, and intend to seek one or more collaborators to commercialize the product in additional markets. Our patents include claims covering formulations, methods of manufacturing and use of elastases, providing protection in the United States and European Union through 2028, with potential extension through 2032 in the United States.

## **Our Strengths**

We believe our company and PRT-201 possess the following attributes that increase the likelihood that we will be successful in developing and commercializing PRT-201:

- *Entering Phase 3 trials for radiocephalic AVF placement.* We plan to conduct our Phase 3 clinical trials in radiocephalic AVF placement using a 30 microgram dose of PRT-201, the population and dose in which, in a non prespecified analysis, we observed an improvement in primary unassisted patency with PRT-201 in our Phase 2 trial.
- *Phase 3 endpoints same as our Phase 2 trial.* The primary endpoint in our Phase 3 trial, primary unassisted patency, will be the same as we used in our Phase 2 trial. In addition, our secondary endpoint (secondary patency) and tertiary endpoints (unassisted maturation, use for hemodialysis and average procedure rates) in our Phase 3 trial were all endpoints in our Phase 2 trial. In April 2013, we held an end of Phase 2 meeting with the FDA during which we confirmed elements of our Phase 3 development plan, including the primary endpoint.

- *Safety profile supports approval.* Based on results from our clinical trials and preclinical studies, we believe PRT-201, which is administered once and only acts locally, has demonstrated a safety profile that will support approval if our planned Phase 3 clinical program is successful. Because PRT-201 is administered in a one-time, local application and is inactivated by antiproteases in the blood, there is no systemic activity. In clinical trials assessing safety, there were no material increases in adverse events in the PRT-201 treatment groups as compared to placebo and no material findings related to physical examinations or clinical laboratory testing including chemistry, hematology and coagulation panels or antibodies to PRT-201. At our end of Phase 2 meeting with the FDA, we confirmed that we do not need to conduct any additional preclinical studies to support a BLA filing.
- *Unmet medical need.* While AVFs are considered the most desirable form of vascular access by the medical community, they are also associated with high failure rates, a serious complication for hemodialysis patients that results in substantially higher healthcare costs. A 2014 publication estimated the total cost of managing hemodialysis vascular access dysfunction in the United States to be approximately \$2.9 billion annually. We are not aware of any approved preventative treatments to reduce AVF failure rate. PRT-201 has received fast track designation from the FDA, which is designed to facilitate the development and expedite the review of drugs to treat serious conditions and fill an unmet medical need. We believe PRT-201 reduces vascular access failure in patients with chronic kidney disease, or CKD, undergoing hemodialysis and, if approved, could become the standard of care by reducing the cycle of interventions, improving patient outcomes and reducing the overall burden on patients and the healthcare system
- *Substantial and readily-addressable market opportunity.* If PRT-201 is approved, we intend to commercialize this product in the United States and potentially certain European countries ourselves with a specialty hospital sales force, focused primarily on vascular surgeons, and intend to seek one or more collaborators to commercialize the product in additional markets. We estimate a sales force of approximately 75-100 representatives will enable us to call on the approximately 1,300 hospitals that account for more than 90% of the AVF surgical placements performed in the United States annually. We believe PRT-201 will be supported by key stakeholders, including referring nephrologists, patient advocacy groups, large dialysis organizations and payors. We believe PRT-201 will be reimbursed adequately as costs related to AVF surgical placement, which is typically performed in the hospital outpatient setting, are not included in the ESRD bundle, the single bundled payment from Medicare for a number of the costs of hemodialysis treatments, medications, labs and supplies for patients with end stage renal disease.
- *Experienced team.* Our executive management team has extensive experience in the renal and vascular disease fields through their substantial involvement in companies such as Abbott, GelTex, Genzyme, Glaxo, and Merck. Our Chief Executive Officer and Chief Medical Officer were senior executives at GelTex, a biopharmaceutical company, where they played leading roles in the development and commercialization of Renagel, a treatment for hemodialysis patients that led to Genzyme's acquisition of GelTex for more than \$1 billion.

## Our Strategy

Our strategy is to develop and commercialize PRT-201 for patients suffering from renal and vascular diseases, beginning with patients with CKD undergoing surgical creation of a radiocephalic AVF. Key elements of our strategy include our plans to:

- *Complete clinical development of PRT-201 and seek regulatory approval in the United States in its lead indication.* We plan to commence our first Phase 3 clinical trial of PRT-201 for patients with CKD undergoing creation of a radiocephalic AVF in the third quarter of 2014. Prior to completing enrollment in the first Phase 3 trial, we will initiate our second Phase 3 trial in the first half of 2015. If the results of the first Phase 3 trial are sufficiently compelling, we intend to meet with the FDA to discuss the possibility of submitting a BLA supported by the single Phase 3 trial and may decide to submit a BLA to the FDA prior to completing the second Phase 3 trial.

- *Commercialize PRT-201 directly in the United States.* If PRT-201 is approved by the FDA, we intend to commercialize it ourselves in the United States with a specialty hospital sales force focused primarily on vascular surgeons. There are approximately 2,800 vascular surgeons in the United States. In 2011, according to the U.S. Renal Data System 2013 Annual Data Report, there were approximately 395,000 hemodialysis patients in the United States at the end of the year. Based on various third-party sources, we estimate that approximately 130,000 AVFs are placed annually. We believe a specialty hospital sales force of approximately 75-100 representatives will enable us to call on the approximately 1,300 hospitals that account for more than 90% of the AVF surgical placements performed in the United States annually. We believe that PRT-201's potential benefits to patients undergoing surgical creation of an AVF will result in its broad adoption.
- *Undertake clinical development of PRT-201 in Europe and establish partnerships for commercialization of PRT-201 in all or parts of Europe.* We are currently evaluating our existing clinical program to support filing in Europe. We may, based on additional data including the data from our Phase 3 clinical trials in the United States and if sufficient funds become available, choose to conduct a clinical trial of PRT-201 in Europe. We estimate that there are approximately 316,000 hemodialysis patients in Europe. Prior to enrolling our first patient in Europe, we plan to formally seek guidance from the European Medicines Agency, or EMA, regarding its requirements for regulatory approval. We expect results from this trial to be available two to three years after the first patient is enrolled. If this European trial successfully meets its primary endpoint and depending on the guidance obtained from the EMA, we would expect to submit a Marketing Authorization Application, or MAA. If PRT-201 is approved by the EMA, we intend to commercialize it in some European countries with our own specialty hospital sales force and/or with a commercial partner in the other European countries. Like in the United States, we intend to target both vascular surgeons who create AVFs as well as key referring nephrologists.
- *Pursue additional indications for PRT-201.* We believe that our Phase 2 clinical data support further development of PRT-201 in brachiocephalic AVF placement. We may, based on additional data including the data from our Phase 3 clinical trials and if sufficient funds become available, study the effects of a 30 microgram dose of PRT-201 versus placebo on brachiocephalic AVFs. If this trial successfully meets its primary endpoint, we would expect to submit a supplemental BLA, or sBLA, to the FDA and a supplemental MAA, or sMAA, to the EMA. Further, if sufficient funds become available and after reviewing the results from our Phase 3 clinical trials, we may commence a clinical trial of PRT-201 in patients undergoing placement of an arteriovenous graft, or AVG. We believe PRT-201's potential to reduce neointimal hyperplasia could offer a significant medical benefit in these patients.
- *Establish partnerships for development and commercialization of PRT-201 in Japan and other Asian countries.* We estimate that there are approximately 295,000 patients on hemodialysis in Japan and more than 750,000 throughout all of Asia. Approximately 90% of Japanese hemodialysis patients receive AVFs. We may enter into collaborations for the development and commercialization of PRT-201 in Asia.
- *In-license or acquire additional product opportunities.* We plan to search for additional product opportunities that could be sold and marketed by the specialty hospital sales force required to successfully launch PRT-201 in the United States if it is approved for marketing.

## **Background on Hemodialysis**

Healthy kidneys serve many functions, including removing waste and excess water, helping to control blood pressure and keeping electrolytes, such as sodium and potassium, in balance. Patients with CKD, have lost most or all kidney function, most commonly due to diabetes or hypertension. Kidney disease is progressive and once a patient has reached end-stage CKD, the kidneys are no longer able to remove waste and fluids from the body. At this point, some form of renal replacement therapy is required, such as hemodialysis, in which blood is processed by a hemodialysis machine, peritoneal dialysis, a process using a



cavity in the abdomen called the peritoneum as a membrane across which fluids are exchanged from the blood, or kidney transplant.

According to the U.S. Renal Data System 2013 Annual Data Report, in 2011 there were approximately 395,000 hemodialysis patients in the United States, and an incremental 104,000 patients initiated hemodialysis in the United States. As reported by Fresenius Medical, a major provider of hemodialysis services and renal care products, there are approximately 316,000 hemodialysis patients in Europe, 295,000 hemodialysis patients in Japan and 2 million hemodialysis patients worldwide, with an annual worldwide growth rate of 6-7%.

Hemodialysis is the most common form of treatment for end-stage CKD. Hemodialysis is a chronic therapy performed by cannulating, or piercing, a vein with a large bore needle so that blood can be pumped through a hemodialysis machine, which removes waste and excess fluid normally excreted by the kidney. The cleansed blood is then returned to the same vein via a second needle. A hemodialysis session typically lasts three to four hours and is performed three times a week in an outpatient dialysis clinic.

To enable sufficient blood to pass through the hemodialysis machine to complete treatment within four hours, a vein must have blood flow of at least 500 milliliters per minute. The arm is the most convenient location for accessing the blood stream on a recurring basis, but blood flow in the arm is approximately 50 milliliters per minute. Therefore, most hemodialysis patients undergo a surgical procedure in which a surgeon establishes a direct connection between an artery and a vein to create a high flow circuit of sufficient diameter, most often in an arm. The direct artery-vein connection effectively bypasses the capillary circulation in the hand and leads to a process known as maturation, where the internal diameter, or lumen, of the vein and blood flow increase over a period of weeks, resulting in a lumen diameter greater than 4 millimeters and blood flow of 500-2,000 milliliters per minute in successful cases.

The gold standard for vascular access is an AVF, in which a surgeon transects a vein in the arm and sutures it to the side of a nearby artery. AVFs are preferred because they are less prone to patency loss than arteriovenous grafts, or AVGs; approximately 50% of AVFs and up to 75% of AVGs will lose primary patency and 20-30% of AVFs and 28-35% of AVGs will lose secondary patency in the first year after surgical placement. As compared to AVGs, AVFs require approximately 40% fewer interventional or surgical procedures and suffer from a rate of vascular access infection that is 54% lower. Patients dialyzing with an AVF have lower rates of thrombosis and hospitalization, longer survival, reduced mortality and lower cost of care. Beyond the substantial medical advantages of an AVF, available data from the U.S. Renal Data System show that patients who dialyze with an AVF cost Medicare approximately \$15,000 less annually than patients who dialyze with an AVG and approximately \$25,000 less annually than patients who dialyze with a catheter. According to published data, approximately 60% of hemodialysis patients in the United States dialyze with an AVF compared to 67-83% of patients in the major European countries and approximately 90% of patients in Japan.

Based on various third-party sources, we estimate there are approximately 130,000 AVFs created in the United States annually. There are a limited number of potential artery-vein combinations in the arm that can be used to create an AVF, principally the following:

- radiocephalic AVF at the wrist (radial artery sutured to cephalic vein), which we estimate is created in 40% of new AVF placements;
- brachiocephalic AVF at the elbow (brachial artery sutured to cephalic vein), which we estimate is created in 50% of new AVF placements; and
- brachio basilic AVF in the upper arm (brachial artery sutured to basilic vein), which we estimate is created in 10% of new AVF placements.

The medical community endorses radiocephalic AVFs as the optimal form of vascular access and the recommended first choice for new hemodialysis patients. Creating the vascular access site at the wrist preserves

the potential future use of other access further up in the arm, is simpler to create, and is less likely to create steal syndrome where the diversion of flow through the AVF reduces blood to the hand. The Kidney Disease Outcome Quality Initiative Guidelines, or KDOQI Guidelines, authored by the National Kidney Foundation, or NKF, specifically recommend starting with a radiocephalic AVF if possible, stating that "starting [closer to the hand] and moving [further up the arm] provides for the possibility of preserving as many potential sites as possible for future access creation." If a radiocephalic AVF must be abandoned, a surgeon can create a new vascular access higher up the arm, most likely a brachiocephalic AVF. However, if a brachiocephalic AVF is placed first, the surgeon cannot later move down that same arm to create a radiocephalic AVF because the cephalic vein has already been transected for use in the brachiocephalic AVF.

Radiocephalic AVFs suffer from high rates of patency loss and maturation failure, with up to 70% of AVFs in the wrist being subject to patency loss within twelve months after their surgical placement. Some patients never receive a radiocephalic AVF because the surgeon believes the risk of failure is too high for those patients. These patients will typically undergo placement of an AVF higher up on the arm and permanently lose at least one of their access sites. We believe that the number of radiocephalic AVFs created annually may rise significantly if PRT-201 improves outcomes and allows vascular surgeons to create radiocephalic AVFs in sites that they previously considered to pose an unacceptably high risk of failure.

The second choice for vascular access after AVF is an AVG in which a surgeon connects an artery and vein using a synthetic tube. Based on reported data, approximately 20% of hemodialysis patients in the United States dialyze with an AVG, compared to approximately 5-12% of patients in the major European countries and approximately 7% of patients in Japan.

The least desirable type of vascular access is a catheter, a plastic tube that is placed directly through the skin into a vein, typically via an incision in the neck enabling placement of the catheter into a large vein that leads directly to the heart. The catheter connects the patient's vasculature to the hemodialysis machine. Because the catheter penetrates the skin continuously, it is subject to a high risk of infection and increased mortality. One of the primary goals of hemodialysis care is to keep patients off catheters. However, patients most often initiate hemodialysis through a catheter until an AVG or AVF is ready to be used, and are dialyzed temporarily through a catheter when the AVF or AVG they have been using fails and a new one has to be created. Approximately 20% of hemodialysis patients in the United States dialyze with a catheter, compared to 10-28% of patients in the major European countries and 2% of patients in Japan, based on published data.

### **Established Medical Need**

The need to improve vascular access outcomes is well established in the hemodialysis community. The health-related and economic cost of creating and maintaining vascular access for hemodialysis has led to a global effort to address the problem. Over the last ten years, the NKF has established guidelines in an effort to increase the use of AVFs while reducing the rate of complications, mostly through the identification and promulgation of best practices. The National Institutes of Health joined the effort in 2000 with the creation of a multi-center consortium of medical centers, the Dialysis Access Clinical Trials Consortium to coordinate the testing of new treatments designed to improve AVF and AVG outcomes. The intensity of these efforts increased markedly in 2004, when the Centers for Medicare and Medicaid Services, or CMS, reacting to health and economic data, announced the "Fistula First" initiative to increase the use of AVFs while reducing complications. According to Fistula First, AVFs should be considered for every patient needing hemodialysis because AVFs last longer than AVGs, require fewer surgical and endovascular interventions, are associated with lower rates of infection, hospitalization and death, and are less costly. As a result of these efforts, AVF use has approximately doubled since 2004 to 60% of United States hemodialysis patients.

A major problem with AVFs and AVGs is patency loss, in which the access experiences either a significant or complete reduction in blood flow, precluding hemodialysis and placing the access at risk of abandonment. However, the increased use of AVFs has led to a concurrent increase in AVF patency loss as AVFs are placed in patients with higher risks of AVF failure, such as the elderly, diabetics or patients with smaller blood vessels. Additionally, physicians have become more aggressive in monitoring and intervening earlier upon AVFs in an attempt to treat patency loss before it results in abandonment of that access site. These factors have resulted in an approximate doubling in the rate of AVF interventions in less than a decade.

We are not aware of any approved preventative measures to reduce the rate of vascular access patency loss, and the clinical implications of patency loss are severe. An episode of patency loss must be addressed urgently to restore blood flow, enable the patient to resume hemodialysis and avoid access abandonment. Treatment of patency loss typically involves an outpatient procedure, either an endovascular intervention, such as balloon angioplasty, stenting or thrombectomy, or a surgical revision.

Procedures to address patency loss are invasive, painful, and associated with a number of complications, and there are a number of problems associated with them:

- *The procedures are not always successful in restoring patency.* Procedures to address AVF patency loss are unsuccessful up to 27% of the time. When these procedures are unsuccessful or the physician determines that a procedure to restore patency is futile, the access site must be abandoned, resulting in the urgent need for catheter placement to enable hemodialysis. Recent data indicate that hemodialysis patients who switch from a permanent vascular access to a catheter have a mortality rate that is double those who remain on a permanent access. Access abandonment also results in surgical placement of a new AVF or AVG, reducing the number of future access sites available to the patient.
- *The procedures often fail to provide a durable benefit, resulting in a cycle of interventions for the patient.* Recent data indicate that 50% of AVFs that undergo angioplasty to treat patency loss experience another episode of patency loss within 12 months, resulting in the need for additional procedures to restore patency. AVF patients in the United States on average require greater than 1.5 procedures per year, each of which typically costs Medicare between \$5,000 and \$13,000. A United States hospital recently published data indicating that maintaining a radiocephalic AVF can cost on average more than \$17,000 in the first year after surgical placement. A 2014 publication estimated the total cost of managing vascular access dysfunction in the United States to be approximately \$2.9 billion annually.

AVFs and AVGs are also prone to secondary patency loss, in which the access must be abandoned. Patients on hemodialysis must dialyze with a catheter until a new permanent access can be surgically placed and becomes usable for hemodialysis, a process that typically requires a minimum of three months for AVFs. During this time, patients are at a heightened risk of serious infection, hospitalization and death.

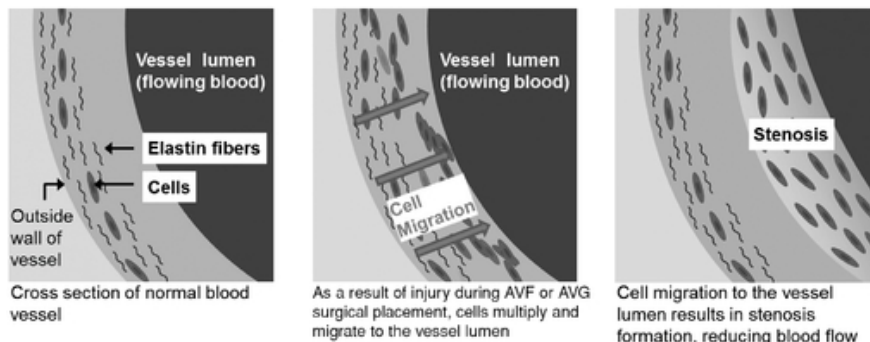
#### **PRT-201**

PRT-201 is a recombinant human elastase under development as a treatment to prevent AVF and AVG patency loss. We expect to initiate the first of two Phase 3 trials for PRT-201 in radiocephalic AVF, our lead indication, in the third quarter of 2014 and initiate the second Phase 3 trial in the first half of 2015.

### Mechanism of Action

AVF patency loss occurs most commonly due to progressive scarring in the wall of the outflow vein near the lumen, resulting in stenosis of the lumen of the vein and obstruction of blood flow in the AVF. This form of vascular scarring is commonly known as neointimal hyperplasia. When surgeons create an AVF they handle and manipulate blood vessels resulting in mechanical vessel injury. Furthermore, after AVF creation the rapid flow of blood from the artery into the outflow vein results in unnatural physiologic changes and mechanical stresses in the vein wall. The response of the vein to this injury and stress results in activation and recruitment of scar forming cells, which multiply and migrate from the outside wall to the inside wall of the blood vessel and produce a thick layer of tissue, creating a narrowing in the vein lumen and a reduction in AVF blood flow. This blood vessel response to injury occurs during the first two to three weeks following vascular surgery and is shown in the following figure.

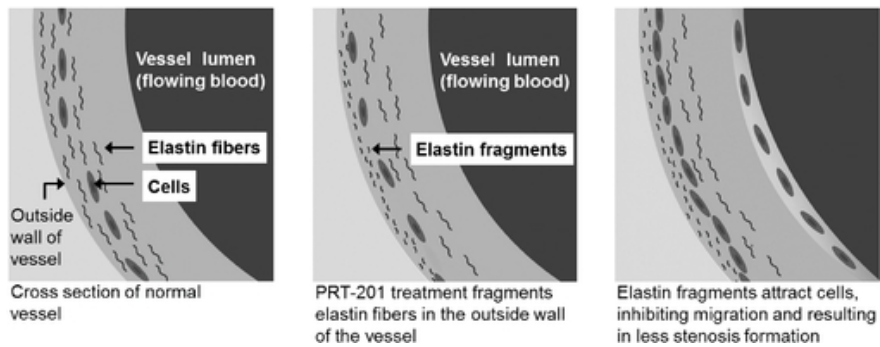
#### Vessel Injury During AVF and AVG Surgical Placement Results in Stenosis Formation



We demonstrated that PRT-201 fragments elastin, a protein present in blood vessel walls. The fragmentation of elastin in the outside wall of the blood vessel is thought to inhibit formation of neointimal hyperplasia thereby reducing the risk of patency loss. Elastase causes localized fragmentation of elastin protein fibers present in blood vessel walls. The elastin fragments generated by elastase are chemoattractants for scar forming cells, meaning that the fragments attract these scar forming cells, inhibiting their migration to the lumen. The cells recognize the elastin fragments via receptors present on the cell surface that bind to specific elastin fragment sub-types. The importance of elastin fragments in vascular biology, including the response to vascular injury has been established in the scientific literature over three decades. Published academic studies conducted in animals provide evidence that fragmentation of elastin in the outer wall of the blood vessels from administration of elastase after vascular injury resulted in a 38-42% reduction in neointimal hyperplasia at 28 days following the surgical procedure. Based on our preclinical *in vivo* and *ex vivo* studies in human vessels, applying PRT-201 to the external surface of the blood vessels generates localized elastin fragments in the outside wall of injured blood vessels. We have established this effect in the doses we plan to advance in our clinical trials. We believe that a one-time, local application of a 30 microgram dose of PRT-201 to the external surface of the vessels during AVF surgical placement can reduce the vascular scarring on the inside of the vessel wall resulting from surgery and thereby reduce the severity of neointimal hyperplasia and the risk of AVF failure. We believe the elastin fragments that are generated by PRT-201 attract scar forming cells to the outside wall of the injured

vessel, reducing their movement to the inside wall of the vessel, thereby inhibiting lumen stenosis. This mechanism is portrayed in the following figure:

### PRT-201 Treatment Inhibits Stenosis Formation



This injury response and the role of elastase-generated fragments are operative in other cardiovascular surgeries, such as bypass, and interventional procedures, such as angioplasty.

### Clinical Development of PRT-201

#### *Our Phase 2 AVF Clinical Trial*

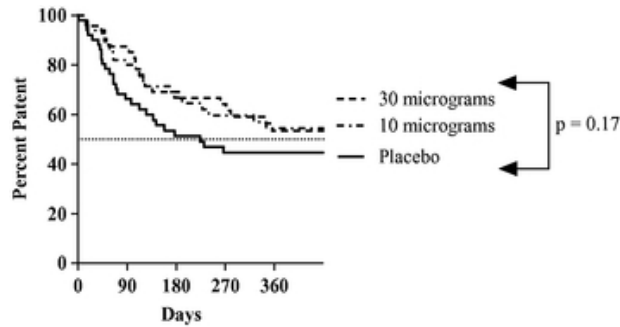
We completed a multicenter, randomized, double-blind, placebo-controlled Phase 2 trial of PRT-201 in AVF that treated 151 patients with CKD undergoing creation of a radiocephalic AVF (n=67) or brachiocephalic AVF (n=84). Patients were treated with PRT-201 at doses of 10 or 30 micrograms or placebo at the time of AVF placement and were followed for up to 12 months.

#### *Primary endpoint*

The primary efficacy endpoint was primary unassisted patency over 12 months. Primary unassisted patency was defined as the time from access creation until the first occurrence of either AVF thrombosis or a procedure, such as balloon angioplasty, to restore or maintain patency.

Both doses of PRT-201 showed a trend toward efficacy, although neither dose met the primary endpoint with statistical significance. Median patency, the time at which 50% of patients in a group lost primary unassisted patency, was 224 days in the placebo group and greater than 365 days in each of the PRT-201 treatment groups indicating patency in the PRT-201 treatment groups was prolonged by PRT-201. Treatment with PRT-201 at 10 and 30 microgram doses was associated with a reduction of 31% and 33%, respectively, in the risk of primary unassisted patency loss. After adjusting for differences in baseline characteristics associated with the risk of primary unassisted patency loss, treatment with PRT-201 at 10 and 30 microgram doses was associated with a reduction of 24% and 41%, respectively, in the risk of primary unassisted patency loss. The following Kaplan-Meier curves and table display primary unassisted patency for all AVFs.

**Primary Unassisted Patency—All AVFs**



Note: Prespecified analysis.

The table below shows the primary unassisted patency data in the placebo and PRT-201 treatment groups.

**Reduction in Risk of Primary Unassisted Patency Loss vs. Placebo—All AVFs**

	<b>PRT-201 10 microgram dose</b>	<b>PRT-201 30 microgram dose</b>
Number of Patients	N=51	N=49
Unadjusted Risk vs. Placebo	-31% (p=0.19)	-33% (p=0.17)
Adjusted Risk(1) vs. Placebo	-24% (p=0.35)	-41% (p=0.10)

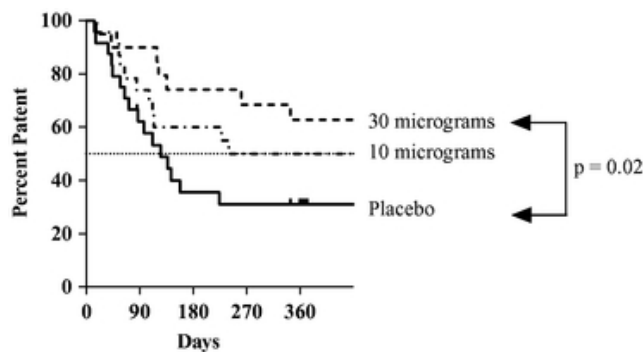
Note: Prespecified analysis.

- (1) Adjusted for differences in baseline characteristics associated with the risk of primary unassisted patency loss between treatment groups using a prespecified Cox regression analysis.

Patients completing 12 months of follow-up in the initial trial were followed in a registry to obtain additional data related to the efficacy endpoints. In this follow-up, the PRT-201 benefit on primary unassisted patency persisted out to 900 days.

**Radiocephalic AVFs.** The benefit of PRT-201 on primary unassisted patency was most pronounced in the subset of patients undergoing placement of a radiocephalic AVF than in the subset of patients undergoing placement of a brachiocephalic AVF or all patients undergoing placement of an AVF. The subset analysis of this endpoint was not prespecified. The following Kaplan-Meier curves and table summarize the reduction in risk of primary unassisted patency loss in the subset of patients with radiocephalic AVFs. Treatment with PRT-201 at doses of 10 and 30 micrograms was associated with a reduction of 41% and 63%, respectively, in the risk of primary unassisted patency loss. Median patency was 125 days in the placebo group and greater than 365 days in the 30 microgram group, indicating a significant improvement in primary unassisted patency.

**Primary Unassisted Patency—Radiocephalic AVFs**



Note: Not prespecified analysis.

**Reduction in Risk of Primary Unassisted Patency Loss vs. Placebo—Radiocephalic AVFs**

	<b>PRT-201 10 micrograms</b>	<b>PRT-201 30 micrograms</b>
Number of Patients	N=23	N=20
Unadjusted Risk vs. Placebo	-41% (p=0.18)	-63% (p=0.02)
Adjusted Risk(1) vs. Placebo	-40% (p=0.20)	-61% (p=0.04)

Note: Not prespecified analysis.

- (1) Adjusted for differences in baseline characteristics associated with the risk of primary unassisted patency loss between treatment groups using a prespecified Cox regression analysis.

*Brachiocephalic AVFs.* The benefit of PRT-201 on primary unassisted patency was less pronounced in the subset of patients undergoing placement of a brachiocephalic AVF. This was in part due to an uneven distribution between brachiocephalic AVF groups in the number of patency loss events occurring in the central veins and cephalic arch, also known as central stenosis, which are remote from the site of the AVF. Central stenoses commonly exist prior to surgery due to the venous anatomy or scarring from a prior hemodialysis catheter, but are typically unmasked following placement of the higher blood flow brachiocephalic AVFs. Since PRT-201 is active locally at the site where it is applied on the AVF, and because we have demonstrated that PRT-201 is not active remotely, we believe that central stenoses are unrelated to PRT-201. Therefore, to correct for this uneven distribution, we conducted a non-prespecified analysis of the primary endpoint in brachiocephalic AVFs which excluded patency loss events due to central stenoses. The following table summarizes the risk of primary unassisted patency loss in brachiocephalic AVFs including and then excluding patency loss events related to central stenoses.

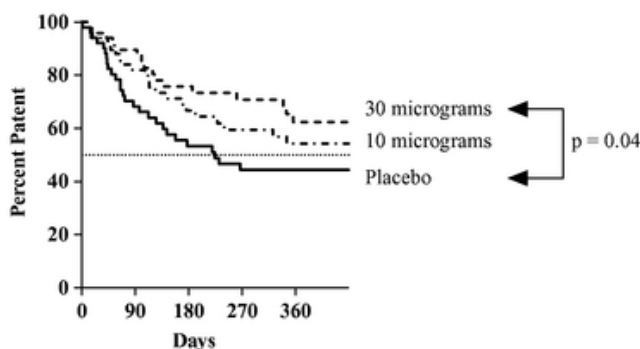
**Reduction in Risk of Primary Unassisted Patency Loss vs. Placebo—Brachiocephalic AVFs**

	<b>PRT-201 10 micrograms</b>	<b>PRT-201 30 micrograms</b>
Number of Patients	N=28	N=29
Unadjusted Risk vs. Placebo	-14% (p=0.72)	+10% (p=0.82)
Unadjusted Risk vs. Placebo Excluding Central Stenoses	-12% (p=0.76)	-26% (p=0.46)

Note: Not prespecified analysis.

We also conducted a non-prespecified analysis across all patients of the primary endpoint correcting for this uneven distribution in central stenoses. The following Kaplan-Meier curves for primary unassisted patency for all AVFs (excluding central stenoses) and table demonstrate a significant reduction in the risk of primary unassisted patency loss for the 30 microgram dose (p=0.04, for the 30 microgram dose) versus placebo. Treatment with PRT-201 at doses of 10 and 30 micrograms was associated with a reduction of 31% and 48%, respectively, in the risk of primary unassisted patency loss. After adjusting for differences in baseline characteristics associated with the risk of primary unassisted patency loss, treatment with PRT-201 at doses of 10 and 30 micrograms was associated with a reduction of 25% and 52%, respectively, in the risk of primary unassisted patency loss.

**Primary Unassisted Patency—All AVFs  
(Excluding Central Stenoses)**



Note: Not prespecified analysis.

**Reduction in Risk of Primary Unassisted Patency Loss vs. Placebo—All AVFs  
(Excluding Central Stenoses)**

	<b>PRT-201 10 micrograms</b>	<b>PRT-201 30 micrograms</b>
Number of Patients	N=51	N=49
Unadjusted Risk vs. Placebo	-31% (p=0.20)	-48% (p=0.04)
Adjusted Risk vs. Placebo(1)	-25% (p=0.33)	-52% (p=0.02)

Note: Not prespecified analysis.

- (1) Adjusted for differences in baseline characteristics associated with the risk of primary unassisted patency loss between treatment groups using a prespecified Cox regression analysis.



In a larger trial of brachiocephalic AVFs, we expect that the occurrence of patency loss due to central stenosis would be evenly distributed between treatment groups. In the Phase 3 clinical trials we have planned, we expect that patency loss due to central stenosis would be rare since we intend to enroll radiocephalic AVF patients exclusively and radiocephalic AVFs rarely suffer from patency loss due to central stenosis because of lower blood flow. In our Phase 2 trial, no radiocephalic AVF in any group lost primary patency due to central stenosis.

*Secondary and other endpoints*

PRT-201 showed results consistent with a beneficial drug effect on multiple secondary efficacy endpoints. The prespecified efficacy endpoints were unassisted maturation, secondary patency, use for hemodialysis and hemodynamically significant lumen stenosis. In addition, we performed a prespecified efficacy analysis of average rate of procedures to restore or maintain AVF patency, a component of our primary endpoint. As with the primary efficacy analyses, we performed a number of prespecified and exploratory analyses of the data from this Phase 2 trial.

- Unassisted maturation.* Maturation is necessary for use of an AVF for hemodialysis. Unassisted maturation was defined as achieving maturation at three months without an intervention. Maturation was assessed using ultrasound measuring blood flow and lumen vein diameter. All ultrasounds were reviewed by a central reader masked to treatment assignment and AVF outcome. Two well-accepted criteria for measuring maturation were used, as shown in the footnotes in the table below. The 30 microgram dose, which we intend to study in our Phase 3 trials, showed statistically significant improvement in maturation at Month 3, with more benefit seen in patients receiving radiocephalic AVFs (figure below) than in patients receiving brachiocephalic AVFs. In the subset of patients with brachiocephalic AVFs, there was a trend toward improvement in unassisted maturation at both the 10 and 30 microgram doses.

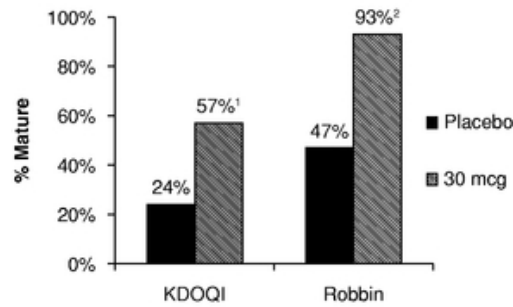
**Unassisted Maturation at Three Months—% of Patients (p-Value vs. Placebo)**

	Placebo	PRT-201 10 micrograms	PRT-201 30 micrograms
<b>All AVFs</b>			
Number of Patients	N=39	N=39	N=37
Percentage Mature NKF-KDOQI(1)	46%	64% (p=0.11)	70% (p=0.03)
Percentage Mature Robbin(2)	67%	87% (p=0.03)	92% (p<0.01)
<b>Radiocephalic AVFs</b>			
Number of Patients	N=17	N=19	N=14
Percentage Mature NKF-KDOQI(1)	24%	37% (p=0.48)	57% (p=0.08)
Percentage Mature Robbin(2)	47%	74% (p=0.17)	93% (p<0.01)
<b>Brachiocephalic AVFs</b>			
Number of Patients	N=22	N=20	N=23
Percentage Mature NKF-KDOQI(1)	64%	90% (p=0.07)	78% (p=0.34)
Percentage Mature Robbin(2)	82%	100% (p=0.11)	91% (p=0.41)

Note: Prespecified analysis.

- National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF-KDOQI) maturation is defined as average vein lumen diameter  $\geq 6$  millimeters and an outflow vein blood flow rate  $\geq 600$  milliliters/minute.
- Robbin maturation is defined as average vein lumen diameter  $\geq 4$  millimeters and an outflow vein blood flow rate  $\geq 500$  milliliters/minute.

## Unassisted Maturation—Radiocephalic AVFs



Note: Prespecified analysis.

(1) p-value=0.08 vs. placebo

(2) p-value<0.01 vs. placebo

- *The average rate of procedures to restore or maintain patency per patient year at risk.* Patients undergoing a procedure often require repeated procedures over time because procedures such as balloon angioplasty can restore blood flow acutely but also damage the blood vessel. These data can be expressed as a procedure rate calculated as the number of days in which procedure to restore or maintain patency was performed per patient divided by the patient's time on the trial. Procedures included thrombectomy, angioplasty, stent deployment and surgical revision. There was a 56% reduction in the rate of procedures in the 30 microgram group versus the placebo group. In the radiocephalic subset there was a 69% reduction in the average rate of procedures in the 30 microgram group versus the placebo group. In the brachiocephalic subset there was a 43% reduction in the average rate of procedure in the 30 microgram group versus the placebo group. Excluding procedures to treat central stenosis, in the brachiocephalic subset there was an 86% reduction in the average rate of procedures in the 30 microgram group versus the placebo group.

## Average Procedure Rate to Restore/Maintain Patency (p-Value vs. Placebo)

	Placebo	PRT-201 10 micrograms	PRT-201 30 micrograms
<b>All AVFs (Prespecified)</b>			
Number of Patients	N=51	N=50	N=48
Procedures per Year	0.9	0.8 (p=0.53)	0.4 (p=0.07)
<b>All AVFs Excluding Central Stenoses (Non-prespecified)</b>			
Number of Patients	N=51	N=50	N=48
Procedures per Year	0.8	0.7 (p=0.44)	0.2 (p<0.01)
<b>Radiocephalic AVFs (Non-prespecified)</b>			
Number of Patients	N=24	N=23	N=20
Procedures per Year	1.0	0.8 (p=0.63)	0.3 (p=0.06)
<b>Brachiocephalic AVFs (Non-prespecified)</b>			
Number of Patients	N=27	N=27	N=28
Procedures per Year	0.7	0.7 (p=0.72)	0.4 (p=0.50)
<b>Brachiocephalic AVFs Excluding Central Stenoses (Non-prespecified)</b>			
Number of Patients	N=27	N=27	N=28
Procedures per Year	0.7	0.7 (p=0.54)	0.1 (p=0.07)

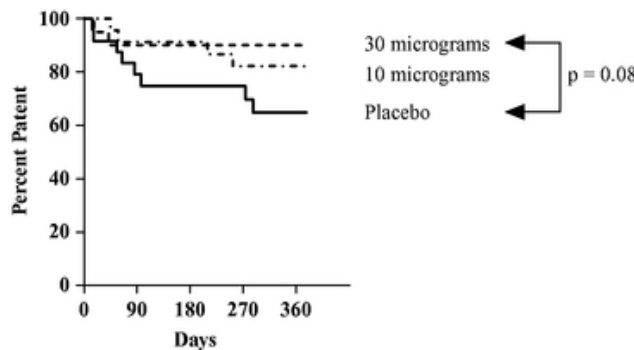
Patients completing 12 months of follow-up in the initial trial were followed in a registry to obtain additional data related to the efficacy endpoints. In this follow up, the PRT-201 benefit on procedure rates persisted out to 900 days as set out in the following table.

**Average Procedure Rate to Restore/Maintain Patency Including Registry Data (p-Value vs. Placebo)**

	Placebo	PRT-201 10 micrograms	PRT-201 30 micrograms
<b>All AVFs (Prespecified analysis)</b>			
Number of Patients	N=51	N=50	N=48
Procedures per Year	0.8	0.8 (p=0.61)	0.3 (p=0.03)
<b>Radiocephalic AVFs (Non-prespecified analysis)</b>			
Number of Patients	N=24	N=23	N=20
Procedures per Year	1.0	0.8 (p=0.47)	0.2 (p=0.03)
<b>Brachiocephalic AVFs (Non-prespecified analysis)</b>			
Number of Patients	N=27	N=27	N=28
Procedures per Year	0.7	0.8 (p=1.00)	0.4 (p=0.40)

- Secondary patency.** Secondary patency loss was defined as abandonment of the AVF, which typically occurs following loss of primary unassisted patency due to thrombosis or failure of a procedure to restore patency and leads to additional surgery to create a new vascular access. We observed no significant differences in the risk of secondary patency loss in the overall AVF population or the subset of patients receiving brachiocephalic AVFs. However, as seen in the Kaplan-Meier curves and table below, a trend toward prolonged secondary patency was seen in patients receiving radiocephalic AVFs. In this non-prespecified subset analysis, treatment with PRT-201 at doses of 10 and 30 micrograms was associated with reductions of 55% and 73%, respectively, in the risk of secondary patency loss.

**Secondary Patency—Radiocephalic AVFs**



Note: Not prespecified analysis.

	PRT-201 10 microgram dose	PRT-201 30 microgram dose
Number of Patients	N=23	N=20
Unadjusted Risk vs. Placebo	-55% (p=0.19)	-73% (p=0.08)

Note: Not prespecified analysis.

Patients completing 12 months of follow-up in the initial trial were followed in a registry to obtain additional data related to the efficacy endpoints. In this follow-up, the PRT-201 benefit on secondary patency in radiocephalic AVFs persisted out to 900 days.

- **Use for hemodialysis.** Use was defined as use of the AVF for hemodialysis at any time without a previous intervention. Although the results were not statistically significant, there was a trend to more patients using the AVF for hemodialysis in the 30 microgram group (69%) compared with the placebo group (53%).
- **Hemodynamically significant lumen stenosis.** Hemodynamically significant lumen stenosis, or narrowing of blood vessels, impairs AVF maturation and contributes to AVF patency loss. Hemodynamically significant stenosis was defined as a 50% or greater stenosis and a significant elevation in peak blood flow velocity across the stenosis detected by ultrasound. Ultrasounds were performed using a standard protocol and reviewed by a central reader masked to treatment assignment and AVF outcome. Although the results were not statistically significant, there was a trend to fewer patients with a hemodynamically significant stenosis in the patients receiving 10 micrograms (30%) and 30 micrograms (39%) of PRT-201 compared with the placebo group (51%) at 6 weeks. Detecting hemodynamically significant stenosis is technically challenging and often confounded by the performance of procedures, such as angioplasty to treat stenosis prior to the ultrasound examination.

*Safety and tolerability*

PRT-201 is administered topically at the vascular access and only acts locally. We have not observed systemic activity or toxicity in our preclinical animal studies, even following intravenous administration at very high multiples of the Phase 2 clinical trial doses. Safety evaluations in Phase 2 included ascertainment of adverse events, physical examinations, ultrasounds of the AVFs and nearby vessels, vital signs and laboratory studies. No significant safety signals were identified. In the trial, patients treated with PRT-201 reported adverse events, the most common of which are summarized in the following table, comparable to placebo. These events were consistent with the medical events experienced by CKD patients undergoing AVF placement surgery. The most common adverse events were AVF incision pain, venous stenosis, AVF thrombosis, steal syndrome and hypoesthesia. Serious adverse events, or SAEs, reported by the investigator as possibly drug-related occurred in two 10 microgram PRT-201 patients (both AVF thrombosis), and two 30 microgram patients (one chest pain and one swelling at the surgical incision). There were no SAEs reported by the investigator as possibly drug-related in the placebo group. There was one SAE reported by the investigator to be drug-related in the 10 microgram PRT-201 group (AVF maturation failure), and there were none in the other treatment groups.

**Number and Proportion (%) of Patients with Common Adverse Events(1)**

<b>N (%)</b>	<b>Placebo N=51</b>	<b>PRT-201 10 micrograms N=51</b>	<b>PRT-201 30 micrograms N=49</b>
Any adverse event	42 (82)	39 (77)	43 (88)
AVF thrombosis	13 (26)	8 (16)	7 (14)
Venous stenosis	10 (20)	7 (14)	8 (16)
Steal syndrome	7 (14)	2 (4)	6 (12)
Hypoesthesia	7 (14)	6 (12)	6 (12)
AVF incisional pain	5 (10)	9 (18)	9 (18)
AVF site complication	5 (10)	4 (8)	4 (8)
Nausea	5 (10)	1 (2)	2 (4)
Peripheral edema	5 (10)	0 (0)	2 (4)
Arterial stenosis	4 (8)	5 (10)	0 (0)
Paresthesia	1 (2)	1 (2)	5 (10)
Pain in extremity(2)	0 (0)	1 (2)	5 (10)

Note: None of the differences between groups were statistically significant.

- (1) Adverse events occurring in at least 10% of placebo or either PRT-201 treatment groups.
- (2) All but one unrelated to limb used in AVF surgery.

### ***Phase 1/2 AVF Clinical Trial***

Our initial clinical trial of PRT-201 was a Phase 1/2, randomized, double-blind, placebo-controlled, dose-escalation safety and exploratory efficacy trial in 66 patients undergoing creation of a radiocephalic or brachiocephalic AVF. Patients were treated with PRT-201 at nine dose levels ranging from 3.3 micrograms to 9 milligrams or placebo at the time of AVF placement and were followed for up to one year. This trial did not meet its primary endpoint, an endpoint we did not pursue in our Phase 2 trial. However, consistent with our mechanism of action that involves partial fragmentation of elastin doses of PRT-201 at 3.3, 10 and 33 micrograms were associated with a trend toward prolonged primary unassisted patency (secondary endpoint  $p=0.66$  in the All Treated population and  $p=0.15$  in the All Treated Minus 3 population), fewer procedures to restore or maintain patency (collected as supportive data) and less hemodynamically significant AVF lumen stenosis (collected as supportive data) compared with placebo treated patients or patients treated with higher PRT-201 doses. Higher doses showed results similar to placebo and no dose met the primary efficacy endpoint with statistical significance. No dose-related increases in adverse events were observed in the trial. Based on the results of this trial, we selected 10 microgram and 30 microgram doses for further study in the Phase 2 trial.

### ***Our Phase 3 Program***

We plan to conduct two randomized, double-blind Phase 3 trials, with staggered start dates, comparing a 30 microgram dose of PRT-201 to placebo. We plan to initiate our first Phase 3 pivotal trial for PRT-201 in patients with CKD undergoing placement of a radiocephalic AVF in the third quarter of 2014. The trials will enroll patients undergoing a surgical procedure to create a radiocephalic AVF. Each Phase 3 trial will enroll approximately 300 patients, for a total of approximately 600 patients, who will be randomized such that twice as many will receive PRT-201 as compared to placebo.

In April 2013, we held an end of Phase 2 meeting with the FDA, during which we confirmed the following key elements of our Phase 3 development plan: (i) the primary efficacy endpoint in our Phase 3 trials, primary unassisted patency, which is the same as our primary endpoint in our Phase 2 trial and suitable for approval of PRT-201 in the United States; (ii) the secondary efficacy endpoint in our Phase 3 trials, secondary patency, which was a secondary endpoint in our Phase 2 trial, could be acceptable for inclusion in the approved product labeling in the United States if we hit statistical significance on both the primary endpoint and the secondary endpoint, and possibly even if we do not hit statistical significance on the secondary endpoint; (iii) the total number of patients expected to be treated through our Phase 3 trial will provide a sufficient safety database to support a BLA filing; (iv) we do not need to conduct additional preclinical studies prior to conducting its Phase 3 clinical trials or to support a BLA filing; and (v) we have Phase 3-ready drug substance and drug product.

We intend to begin enrolling patients in our first Phase 3 trial beginning in the third quarter of 2014. Each patient will be followed for 12 months. We expect that results will be available in 2017.

Our Phase 3 trials will be conducted at sites in the United States with the second trial potentially including Canadian sites. In addition to collecting data on the primary and secondary endpoints, the Phase 3 clinical trials will collect information related to the tertiary endpoints of maturation, use for hemodialysis and the rate of procedures to restore or maintain patency. Patients who consent will be enrolled in a patient registry to obtain long-term follow-up efficacy information.

We have designed each Phase 3 trial to have over 95% power. If the results of the first Phase 3 trial are sufficiently compelling, we intend to meet with the FDA to discuss the possibility of submitting a BLA, supported by the single Phase 3 trial and may decide to submit a BLA to the FDA prior to completing the second Phase 3 trial.

## **Preclinical Development**

We have conducted an extensive preclinical program to evaluate the safety and tolerability of single doses of PRT-201 administered locally in animal models of AVF and AVG placement, by percutaneous and endovascular injection in animal models of PAD, as well as intravenously. We have conducted preclinical studies in multiple species at doses up to 50 milligrams of PRT-201, which is over 1500 times higher than the dose we intend to study in our planned Phase 3 clinical trials. We observed no systemic activity or toxicity for PRT-201 in any of our preclinical studies. We observed no toxicity in any of the doses that we subsequently studied or plan to study in humans. Only local toxicity was observed at surgical sites at high doses (10 and 50 milligrams, which is over 300-1500 times higher than the dose we intend to study in our planned Phase 3 clinical trials). These changes were reversible, with normal wound healing observed at 14 days except at the highest (50 milligrams) dose, in which there were some mild persistent changes in the jugular vein and subcutaneous tissue. Normal wound healing was observed in all the AVF studies in rabbits at doses up to 10 milligrams and in all the AVG studies in dogs and pigs at doses up to 20 milligrams (the highest doses tested).

In our preclinical studies, we observed dose-dependent activity of PRT-201 on elastin removal as studies have established correlates with a reduction in neointimal hyperplasia.

## **Other Programs, Indications and Trials**

### ***Other AVF Trials***

#### *European clinical program*

We are currently evaluating our clinical program to support filing in Europe. We may, based on additional data including the data from our Phase 3 clinical trials in the United States and if sufficient funds become available, choose to conduct a clinical trial of PRT-201 in Europe. Prior to initiating a European clinical trial, we plan to formally seek guidance from the European Medicines Agency, or EMA, regarding their requirements for regulatory approval.

#### *Brachiocephalic AVF*

We believe that our Phase 2 clinical data supports further development of PRT-201 in brachiocephalic AVF placement. We may, based on additional data including the data from our Phase 3 clinical trials and if sufficient funds become available, study the effects of a 30 microgram dose of PRT-201 versus placebo on brachiocephalic AVFs. Prior to initiation of this trial, we expect to seek guidance from the FDA regarding trial design.

### ***Arteriovenous Grafts***

An arteriovenous graft, or AVG, is a surgical procedure in which a surgeon places a synthetic tube to connect a vein and an artery. We conducted a Phase 1/2 randomized, double-blind, placebo-controlled, dose-escalation trial in 89 patients undergoing placement of an AVG. Patients were treated with placebo or eight different doses of PRT-201 ranging from 10 micrograms to 9 milligrams at the time of AVG placement and were followed for up to one year. Those patients who had not lost secondary patency were subsequently enrolled in a registry to obtain additional follow-up information on the AVG.

The primary outcome measure was safety. Adverse events were consistent with the medical conditions experienced by patients with CKD undergoing AVG surgery and showed no significant differences between groups. Some of the data showed indications of efficacy, especially in secondary patency, which is an approvable endpoint for hemodialysis access, for the groups treated with PRT-201 at doses of 10 micrograms and 30 micrograms.

After reviewing the results from our first Phase 3 clinical trial and if sufficient funds become available, we may commence a clinical trial of PRT-201 in patients undergoing placement of an AVG.

### ***Peripheral Artery Disease***

In addition to vascular access indications, we are investigating PRT-201 as a treatment for patients with symptomatic peripheral artery disease, or PAD. Patients with lower extremity PAD suffer from stenosis formation in the arteries providing blood to the legs. These patients typically present with exercise-induced leg pain, a condition known as intermittent claudication. Patients with claudication are unable to adequately maintain their activities of daily living because they quickly experience pain that can be resolved only through rest. Severe cases result in critical limb ischemia, or lack of oxygen, and the possibility of amputation. PAD is a global problem affecting a large number of people throughout the industrialized world. Approximately 8 million Americans suffer from PAD.

Patients with early stage PAD typically undergo lifestyle management such as smoking cessation, weight reduction and/or diabetes management, and treatment with oral medications. Approximately 350,000 patients in the United States do not respond to lifestyle management and have worsening symptoms, resulting in the need for endovascular procedures, typically balloon angioplasty with or without stenting. While these procedures work acutely to restore blood flow, they suffer from poor long-term durability, resulting in the need for repeat procedures.

We believe that PRT-201 may improve the outcomes associated with angioplasty procedures, resulting in prolonged intervention-free patency while eliminating the need for permanent implant of a stent. Our initial PAD clinical trial is an ongoing Phase 1, open-label, dose-escalation safety/technical feasibility trial in 16 patients undergoing balloon angioplasty of an occluded or partially occluded superficial femoral or popliteal artery in the leg. Following successful angioplasty, patients are treated with PRT-201 via an FDA-cleared drug delivery catheter that allows PRT-201 to be administered locally in the outer layer of the artery, which is called the adventitia. Patients are being followed for up to 12 months. We expect data from this trial to be available in the second half of 2015.

### **Manufacturing and Supply**

We depend on third-party contract manufacturers for the production of PRT-201. Our active pharmaceutical ingredient, or API, is produced at our contract manufacturer, Lonza AG. PRT-201 finished product is produced at our contract fill/finish provider, Jubilant HollisterStier. Release testing and stability for API and finished product are performed at PPD, Inc. We used API manufactured at Lonza to create finished product that was used in our Phase 2 AVF clinical trial and will be used for our Phase 3 clinical trials. We also plan to use API manufactured at Lonza for our commercial launch and future trials.

In preparation for commercial launch, we modified our finished product for our Phase 3 trials in order to facilitate ease of administration and fill and finish at 30 microgram doses. The modified finished product is reconstituted with sterile water to create a dosing solution containing 30 micrograms of PRT-201. We demonstrated that the modified finished product had the same elastase activity as the previous finished product using synthetic and natural elastin substrates and documented the same elastin removal from blood vessels following ex vivo treatments. The modified finished product formulation was similar to the previous finished product formulation in maintaining the health and viability of live cells in culture. These data suggest the modified finished product will have the same efficacy and safety as the previous finished product in clinical trials.

At our end of Phase 2 meeting, the FDA confirmed that our API and modified finished product are acceptable for Phase 3 clinical trials. We have already manufactured finished product for the AVF Phase 3 clinical trials.

In anticipation of a potential BLA filing, we plan to manufacture a minimum of three batches of API and of finished product as part of process validation and to test these batches for stability with a goal of establishing a commercial shelf-life of at least two years for finished product and a longer expiry for API.

## **Sales and Marketing**

Our commercialization strategy is to develop PRT-201 into a leading therapy worldwide for the treatment of AVFs and in other renal and vascular diseases.

We have not yet established a sales and marketing organization. Our Chief Executive Officer has significant commercial experience in the industry, including commercial launch experience in the renal market. We intend to recruit an in-house specialty hospital sales force in the United States focused on promoting PRT-201. We plan to target our marketing and sales efforts to vascular surgeons who create AVFs. There are approximately 2,800 vascular surgeons in the United States. We believe a specialty hospital sales force of approximately 75-100 representatives, supported by reimbursement specialists and a medical affairs team, will enable us to call on the approximately 1,300 hospitals that account for more than 90% of the AVF placements performed in the United States annually.

We believe that the market for PRT-201 in the five largest countries in the European Union represents the bulk of the potential European market and that a launch using a direct sales force may be achievable in these markets. If PRT-201 is approved by the EMA, we may commercialize it in some European countries with our own specialty hospital sales force and/or with a commercial partner in the other European countries. We hope to enter into collaborations for the development and commercialization of PRT-201 in Japan and other Asian countries.

We believe PRT-201 will be reimbursed appropriately as costs related to AVF surgical placement, which is typically performed in the hospital outpatient setting, are not included in the ESRD bundle.

## **Intellectual Property**

We strive to protect and enhance the proprietary technology, inventions and improvements that are commercially important to our business, including seeking, maintaining and defending patent rights. We also rely on know-how that may be important to the development of our business. We additionally expect to rely on regulatory protection afforded through data exclusivity, market exclusivity and patent term extensions where available.

Our commercial success may depend in part on our ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to our business; to defend and enforce our patents and to operate without infringing the valid enforceable patents and proprietary rights of third parties.

Our ability to prevent third parties from making, using, selling, offering to sell or importing competing products to ours, including a competitor to PRT-201, depends on the scope of our patents. We have several patents and patent applications relating to the PRT-201 formulation and its therapeutic uses, and possess substantial know-how relating to the development and commercialization of PRT-201. We cannot be sure that any of our pending patent applications or future patent filings will lead to the issuance of new patents, nor can we be sure that any of our existing patents or any patents that may be granted to us in the future will be adequate to protect our market.

We plan on pursuing in-licensing opportunities to develop, strengthen and maintain our proprietary position in our field. We expect to use trademark protection for our products as they are marketed.



## **Patents**

We own 18 issued patents and 27 pending patent applications, two of which have been allowed. The patents and applications primarily fall into two families, a first relating to the PRT-201 formulation and its manufacture and use, as well as other formulations of elastases (the "formulation family"), and the second relating to certain therapeutic uses of PRT-201, and associated systems and kits that include a catheter and are suitable for a subset of those therapeutic uses (the "therapy family"). The formulation family includes one issued United States patent, one issued European patent, additional patents issued in Israel and New Zealand, and patent applications pending in several other major jurisdictions worldwide, including Japan, China, South Korea, Brazil, Mexico, Russia, India, Europe and the United States. The expected expiration date for any patents that have issued or may issue from the formulation family is December 4, 2028, exclusive of possible patent term extension available for one patent covering PRT-201 under the Hatch-Waxman Amendments or comparable provisions in other jurisdictions, except in the United States where we were awarded a patent term adjustment of 199 days due to USPTO delays, taking the expiration date to June 20, 2029. The therapy family includes seven issued United States patents and two issued European patents, and applications pending in the United States, Europe, Canada and Japan. The expected expiration date for any patents that have issued or may issue from the therapy family patents is September 24, 2020, except in the United States where, due to a patent term adjustment, the expected expiration date of two therapy family patents related to systems and kits including elastase and a catheter is June 30, 2021, exclusive of possible patent term extension.

## **Patent Term**

The base term of a U.S. patent is 20 years from the filing date of the earliest-filed non-provisional patent application from which the patent claims priority. The term of a U.S. patent can be lengthened by patent term adjustment, which compensates the owner of the patent for administrative delays at the USPTO. In some cases, the term of a U.S. patent is shortened by terminal disclaimer that reduces its term to that of an earlier-expiring patent.

The term of a U.S. patent may be eligible for patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Act or Hatch-Waxman Amendment, to account for at least some of the time a drug or biologic is under development and regulatory review after the patent is granted. With regard to a drug or biologic for which FDA approval is the first permitted marketing of the active ingredient, the Hatch-Waxman Act allows for extension of protection of one U.S. patent that includes at least one claim covering the composition of matter of an FDA-approved drug or biologic, an FDA-approved method of treatment using the drug or biologic, and/or a method of manufacturing the FDA-approved drug or biologic. The extended protection cannot exceed the shorter of five years beyond the non-extended expiration of the patent or 14 years from the date of the FDA approval of the drug or biologic. Some foreign jurisdictions, including Europe have analogous patent extension provisions, which allow for extension of the protection of a patent that covers a drug approved by the applicable foreign regulatory agency. In the future, if and when PRT-201 receives FDA approval, we expect to apply for patent extension to extend the protection of one of our patents covering PRT-201 or its use.

## **Assignment of Rights and License Agreement**

As successor to Proteon Therapeutics, LLC by merger, we acquired all of the assets of the LLC, including all of the intellectual property rights in the therapy family, entitled "Local, Transcatheter Delivery of Proteases to Reopen Obstructed Biological Conduits." This patent family was originally developed by our founder, Dr. F. Nicholas Franano, at The Johns Hopkins University, or Johns Hopkins, and includes United States patent Nos. 7,063,838; 7,153,505; 7,361,335; 7,632,494; 7,883,699; 8,524,226; 8,562,983; and 8,568,716. Johns Hopkins assigned all of the intellectual property rights to Dr. Franano who in turn assigned the rights to the LLC. Under the terms of the assignment of rights and license agreement

with Johns Hopkins, Dr. Franano reimbursed certain costs of Johns Hopkins and agreed to pay the future costs and expenses of patent prosecution and maintenance, as well as any costs related to infringement. In addition, under the agreement, Dr. Franano granted to Johns Hopkins rights to practice under the intellectual property rights for non-profit purposes. The rights granted to us are further subject to any rights the United States Government may have in inventions that are the subject matter of the acquired patents under the Bayh Dole Act due to its sponsorship of research that led to certain of such inventions. Lastly, Dr. Franano agreed to pay Johns Hopkins a 2.5% royalty on worldwide net sales, including revenues and fees, of products that are covered by the assigned patents. We assumed, and are the successor to, all of Dr. Franano's payment and other obligations to Johns Hopkins.

## **Competition**

The biotechnology and pharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. We face potential competition from many different sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and governmental agencies and public and private research institutions.

Some of our potential competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do. Smaller or early stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

The key competitive factors that will differentiate PRT-201, if approved, are likely to be its efficacy, safety, convenience, price, and the availability of reimbursement from government and other third party payors. Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, more convenient or less expensive than products that we may develop. Our competitors may also obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours.

We are not aware of any therapeutic products approved in the United States or Europe for the prevention of AVF or AVG patency loss. We are aware of other therapies in development for AVF or AVG failure with companies including Shire, Vascular Therapies and Celladon. Other potential competition includes new synthetic grafts, including those that may be developed by companies that currently compete in the graft market, such as W.L. Gore, C.R. Bard and Maquet, as well as tissue engineered grafts, including those in development by Cytograft and Humacyte. PRT-201 could face competition from companies developing technologies to provide a more effective anastomosis, including BioConnect Systems, Caymus Medical, Phraxis, CreatiVasc and TVA Medical. Finally, PRT-201's commercial success could be affected by the development of technologies to improve the outcomes of interventions to restore patency, including stents, stent grafts and drug eluting balloons.

## **Government Regulation and Approval**

### *United States—FDA process*

In the United States, pharmaceutical products are subject to extensive regulation by the FDA. The FDCA, and other federal and state statutes and regulations, govern, among other things, the research, development, testing, manufacture, storage, recordkeeping, approval, labeling, promotion and marketing, distribution, post-approval monitoring and reporting, sampling, and import and export of pharmaceutical products. Biological products used for the prevention, treatment, or cure of a disease or condition of a human being are subject to regulation under the Federal Food, Drug, and Cosmetic Act, the FDCA, except the section of the FDCA which governs the approval of new drug applications, or NDAs. Biological products, such as PRT-201, are approved for marketing under provisions of the Public Health Service Act, or PHSA, via a Biologics License Application, or BLA. However, the application process and requirements

for approval of BLAs are very similar to those for NDAs, and biologics are associated with similar approval risks as drugs. Failure to comply with applicable United States requirements may subject a company to a variety of administrative or judicial sanctions, such as FDA refusal to approve pending NDAs or BLAs, warning or untitled letters, clinical holds, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties, and criminal prosecution.

#### *Approval process*

FDA approval is required before any new unapproved product or a product with certain changes to a previously approved product may be marketed in the United States. FDA approval is required before any new unapproved drug or dosage form, including a new use of previously approved drug, can be marketed in the United States. The steps required to be completed before a drug may be marketed in the United States include:

- preclinical laboratory tests, animal studies, and formulation studies, all performed in accordance with the FDA's Good Laboratory Practice, or GLP, regulations;
- submission to the FDA of an IND application for human clinical testing, which must become effective before human clinical trials may begin and must be updated annually;
- adequate and well-controlled human clinical trials to establish the safety and efficacy of the drug for each indication to FDA's satisfaction;
- submission to the FDA of a BLA;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the drug is produced to assess compliance with current good manufacturing practices or, cGMP, regulations; and
- FDA review and approval of the BLA.

Satisfaction of FDA pre-market approval requirements typically takes many years and the actual time required may vary substantially based upon the type, complexity, and novelty of the product or disease.

Preclinical tests include laboratory evaluation of product chemistry, formulation, and toxicity, as well as animal trials to assess the characteristics and potential safety and efficacy of the product. The conduct of the preclinical tests must comply with federal regulations and requirements, including GLP. The results of preclinical testing are submitted to the FDA as part of an IND along with other information, including information about product chemistry, manufacturing and controls, and a proposed clinical trial protocol. Long term preclinical tests, such as animal tests of reproductive toxicity and carcinogenicity, may continue after the IND is submitted.

A 30-day waiting period after the submission of each IND is required prior to the commencement of clinical testing in humans. If the FDA has neither commented on nor questioned the IND within this 30-day period, the clinical trial proposed in the IND may begin. However, the FDA may within the 30-day time period raise concerns or questions relating to one or more proposed clinical trials and place the clinical trial on a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Accordingly, submission of an IND may or may not result in the FDA allowing clinical trials to commence. A separate submission to an existing IND must also be made for each successive clinical trial conducted during product development.

Clinical trials involve the administration of the investigational new drug or biologic to healthy volunteers or patients under the supervision of a qualified investigator. Clinical trials must be conducted: (i) in compliance with federal regulations; (ii) in compliance with good clinical practice, or GCP, an international standard meant to protect the rights and health of patients and to define the roles of clinical trial sponsors, administrators, and monitors; as well as (iii) under protocols detailing the objectives of the trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. Each protocol involving testing on United States patients and subsequent protocol amendments must be submitted to the FDA as part of the IND.

The FDA may order the temporary, or permanent, discontinuation of a clinical trial at any time, or impose other sanctions, if it believes that the clinical trial either is not being conducted in accordance with FDA requirements or presents an unacceptable risk to the clinical trial patients. The trial protocol and informed consent information for patients in clinical trials must also be submitted to an institutional review board, or IRB, for approval. An IRB may also require the clinical trial at the site to be halted, either temporarily or permanently, for failure to comply with the IRB's requirements, or may impose other conditions.

Clinical trials to support NDAs or BLAs for marketing approval are typically conducted in three sequential phases, but the phases may overlap. In Phase 1, the initial introduction of the drug or biologic into a limited population of healthy human subjects or patients, the product is tested to assess metabolism, pharmacokinetics, pharmacological actions, side effects associated with increasing doses, and, if possible, early evidence on effectiveness. Phase 2 usually involves trials in a limited patient population to evaluate preliminarily the effectiveness of the drug or biologic for a particular indication, dosage tolerance, and optimum dosage, and to identify common adverse effects and safety risks. If a compound demonstrates evidence of effectiveness and an acceptable safety profile in Phase 2 evaluations, Phase 3 trials are undertaken in a larger number of patients, typically at geographically dispersed clinical trial sites, to provide substantial evidence of clinical efficacy, to further test for safety in an expanded and diverse patient population, to permit the FDA to evaluate the overall benefit-risk relationship of the drug or biologic and to provide adequate information for the labeling of the product. In most cases, the FDA requires two adequate and well-controlled Phase 3 clinical trials to demonstrate the efficacy of the drug or biologic. A single Phase 3 trial with other confirmatory evidence may be sufficient in rare instances where the trial is a large multicenter trial demonstrating internal consistency and a statistically very persuasive finding of a clinically meaningful effect on mortality, irreversible morbidity or prevention of a disease with a potentially serious outcome and confirmation of the result in a second trial would be practically or ethically impossible.

After completion of the required clinical testing, an NDA or BLA is prepared and submitted to the FDA. FDA approval of the NDA or BLA is required before marketing of the product may begin in the United States. The NDA or BLA must include, among other things, the results of all preclinical, clinical, and other testing and a compilation of data relating to the product's pharmacology, chemistry, manufacture, and controls. The cost of preparing and submitting an NDA or BLA is substantial. The submission of most NDAs and BLAs is additionally subject to a substantial application user fee, currently exceeding \$2,169,000, and the manufacturer and/or sponsor under an approved new drug application are also subject to annual product and establishment user fees, currently exceeding \$104,000 per product and \$554,000 per establishment. These fees are typically increased annually.

The FDA has 60 days from its receipt of an NDA or BLA to determine whether the application will be accepted for filing based on the agency's threshold determination that it is sufficiently complete to permit substantive review. Once the submission is accepted for filing, the FDA begins an in-depth review. The FDA has agreed to certain performance goals in the review of NDAs and BLAs. Under the Prescription Drug User Fee Act, the FDA has a goal of responding to standard review NDAs within ten months after the 60-day filing review period, but this timeframe is often extended. Most applications for standard review drug or biologic products are reviewed within ten to 12 months; most applications for priority review drugs or biologics are reviewed in six to eight months. Priority review can be applied to drugs that the FDA determines offer major advances in treatment, or provide a treatment where no adequate therapy exists. For biologics, priority review is further limited only for products intended to treat a serious or life-threatening disease relative to the currently approved products. The review process for both standard and priority review may be extended by the FDA for three additional months to consider certain late-submitted information, or information intended to clarify information already provided in the submission.

The FDA may also refer applications for novel drug or biologic products, or drug or biologic products that present difficult questions of safety or efficacy, to an advisory committee—typically a panel that includes clinicians and other experts—for review, evaluation, and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations. Before approving an NDA or BLA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. Additionally, the FDA will inspect the facility or the facilities at which the drug is manufactured. FDA will not approve the product unless compliance with cGMP is satisfactory and the NDA or BLA contains data that provide evidence that the drug or biologic is safe and effective in the indication studied.

After the FDA evaluates the NDA or BLA and the manufacturing facilities, it issues either an approval letter or a complete response letter. A complete response letter indicates that the review cycle of the application is complete and the application is not ready for approval. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional clinical data and/or other significant, expensive, and time-consuming requirements related to clinical trials, preclinical studies and/or manufacturing. The FDA has committed to reviewing resubmissions of the NDA or BLA addressing such deficiencies in two or six months depending on the type of information included. Even if such data are submitted, however, the FDA may ultimately decide that the NDA or BLA does not satisfy the criteria for approval.

An approval letter authorizes commercial marketing of the drug or biologic with specific prescribing information for specific indications. As a condition of NDA or BLA approval, the FDA may require a risk evaluation and mitigation strategy, or REMS, to help ensure that the benefits of the drug or biologic outweigh the potential risks. REMS can include medication guides, communication plans for healthcare professionals, and elements to assure safe use, or ETASU. ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patient registries. The requirement for REMS can materially affect the potential market and profitability of the product. Moreover, product approval may also be conditioned on substantial post-approval testing and surveillance to monitor the product's safety or efficacy. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing.

Changes to some of the conditions established in an approved application, including changes in indications, labeling, or manufacturing processes or facilities, require submission and FDA approval of a new NDA or BLA or NDA or BLA supplement before the change can be implemented. An NDA or BLA supplement for a new indication typically requires clinical data similar to that in the original application, and the FDA uses the same procedures and actions in reviewing NDA or BLA supplements as it does in reviewing NDAs or BLAs. As with new NDAs, the review process is often significantly extended by the FDA requests for additional information or clarification.

#### *U.S. Patent Term Restoration*

Depending upon the timing, duration and specifics of the FDA approval of PRT-201 and any future product candidates, some of our U.S. patents may be eligible for limited patent term extension. The Hatch-Waxman Amendments permit a patent restoration term, often referred to as patent term extension, of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of an NDA or BLA plus the time between the submission date of an NDA or BLA and the approval of that application. Only one patent applicable to an approved drug or biologic is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. The USPTO, in consultation with the FDA, reviews and approves or denies the application for any patent term extension or restoration. In the

future, we intend to apply for extension of patent term for one of our patents covering PRT-201 to add patent life beyond its current expected expiration date.

#### *Post-approval requirements*

Once an NDA or BLA is approved, a product will be subject to certain post-approval requirements. For instance, the FDA closely regulates the post-approval marketing and promotion of drugs and biologics, including standards and regulations for direct-to-consumer advertising, off-label promotion, industry-sponsored scientific and educational activities and promotional activities involving the internet. Drugs and biologics may be marketed only for the approved indications and in accordance with the provisions of the approved labeling. Failure to comply with these requirements can result in adverse publicity, warning letters, corrective advertising, and potential civil and criminal penalties.

Adverse event reporting and submission of periodic reports is required following FDA approval of an NDA or BLA. The FDA also may require post-marketing testing, known as Phase 4 testing, REMS, and surveillance to monitor the effects of an approved product, or the FDA may place conditions on an approval that could restrict the distribution or use of the product. In addition, quality control, drug manufacture, packaging, and labeling procedures must continue to conform to cGMPs after approval. Drug and biologic manufacturers and certain of their subcontractors are required to register their establishments with the FDA and certain state agencies. Registration with the FDA subjects entities to periodic unannounced inspections by the FDA, during which the agency inspects manufacturing facilities to assess compliance with cGMPs. Accordingly, manufacturers must continue to expend time, money, and effort in the areas of production and quality-control to maintain compliance with cGMPs. Regulatory authorities may withdraw product approvals or request product recalls if a company fails to comply with regulatory standards, if it encounters problems following initial marketing, or if previously unrecognized problems are subsequently discovered.

#### *Orphan drug designation*

Under the Orphan Drug Act, the FDA may grant orphan drug designation to drugs or biologics intended to treat a rare disease or condition—generally a disease or condition that affects fewer than 200,000 individuals in the United States. Orphan drug designation must be requested before submitting an NDA or BLA. After the FDA grants orphan drug designation, the generic identity of the drug or biologic and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process. The first NDA or BLA applicant to receive FDA approval for a particular active ingredient to treat a particular disease with FDA orphan drug designation is entitled to a seven-year exclusive marketing period in the United States for that product, for that indication. During the seven-year exclusivity period, the FDA may not approve any other applications to market the same drug or biologic for the same disease, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity. Orphan drug exclusivity does not prevent the FDA from approving a different drug or biologic for the same disease or condition, or the same drug or biologic for a different disease or condition. Among the other benefits of orphan drug designation are tax credits for certain research and a waiver of the NDA or BLA application user fee.

#### *Fast track designation and accelerated approval*

The FDA is required to facilitate the development, and expedite the review, of drugs or biologics that are intended for the treatment of a serious or life-threatening disease or condition for which there is no effective treatment and which demonstrate the potential to address unmet medical needs for the condition. Under the fast track program, the sponsor of a new drug or biologic candidate may request that the FDA designate the candidate for a specific indication as a fast track drug or biologic concurrent with, or after, the filing of the IND for the candidate. The FDA must determine if the drug or biologic candidate qualifies

for fast track designation within 60 days of receipt of the sponsor's request. Unique to a fast track product, the FDA may initiate review of sections of a fast track product's NDA or BLA before the application is complete. This rolling review is available if the applicant provides, and the FDA approves, a schedule for the submission of the remaining information and the applicant pays applicable user fees. However, the FDA's time period goal for reviewing an application does not begin until the last section of the NDA or BLA is submitted. Additionally, the fast track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Any product submitted to the FDA for marketing, including under a fast track program, may be eligible for other types of FDA programs intended to expedite development and review, such as accelerated approval. Drug or biological products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval, which means the FDA may approve the product based upon a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments.

In clinical trials, a surrogate endpoint is a measurement of laboratory or clinical signs of a disease or condition that substitutes for a direct measurement of how a patient feels, functions, or survives. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. A drug or biologic candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or confirm a clinical benefit during post-marketing studies, will allow the FDA to withdraw the drug or biologic from the market on an expedited basis. All promotional materials for drug candidates approved under accelerated regulations are subject to prior review by the FDA.

#### *Pediatric information*

Under the Pediatric Research Equity Act, or PREA, NDAs or BLAs or supplements to NDAs or BLAs must contain data to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the drug is safe and effective. The FDA may grant full or partial waivers, or deferrals, for submission of data. Unless otherwise required by regulation, PREA does not apply to any drug for an indication for which orphan designation has been granted.

#### *Additional controls for biologics*

To help reduce the increased risk of the introduction of adventitious agents, the PHSA emphasizes the importance of manufacturing controls for products whose attributes cannot be precisely defined. The PHSA also provides authority to the FDA to immediately suspend licenses in situations where there exists a danger to public health, to prepare or procure products in the event of shortages and critical public health needs, and to authorize the creation and enforcement of regulations to prevent the introduction or spread of communicable diseases in the United States and between states.

After a BLA is approved, the product may also be subject to official lot release as a condition of approval. As part of the manufacturing process, the manufacturer is required to perform certain tests on each lot of the product before it is released for distribution. If the product is subject to official release by the FDA, the manufacturer submits samples of each lot of product to the FDA together with a release protocol showing a summary of the history of manufacture of the lot and the results of all of the manufacturer's tests performed on the lot. The FDA may also perform certain confirmatory tests on lots of some products, such as viral vaccines, before releasing the lots for distribution by the manufacturer. In addition, the FDA conducts laboratory research related to the regulatory standards on the safety, purity, potency, and effectiveness of biological products. As with drugs, after approval of biologics, manufacturers must address any safety issues that arise, are subject to recalls or a halt in manufacturing, and are subject to periodic inspection after approval.

### *Biosimilars*

The Biologics Price Competition and Innovation Act of 2009, or BPCIA, creates an abbreviated approval pathway for biological products shown to be highly similar to or interchangeable with an FDA-licensed reference biological product. Biosimilarity sufficient to reference a prior FDA-approved product requires that there be no differences in conditions of use, route of administration, dosage form, and strength, and no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency. Biosimilarity must be shown through analytical studies, animal studies, and at least one clinical trial, absent a waiver by the Secretary. A biosimilar product may be deemed interchangeable with a prior approved product if it meets the higher hurdle of demonstrating that it can be expected to produce the same clinical results as the reference product and, for products administered multiple times, the biologic and the reference biologic may be switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic. No biosimilar or interchangeable products have been approved under the BPCIA to date. Complexities associated with the larger, and often more complex, structures of biological products, as well as the process by which such products are manufactured, pose significant hurdles to implementation which are still being evaluated by the FDA.

A reference biologic is granted twelve years of exclusivity from the time of first licensure of the reference product, and no application for a biosimilar can be submitted for four years from the date of licensure of the reference product. The first biologic product submitted under the abbreviated approval pathway that is determined to be interchangeable with the reference product has exclusivity against a finding of interchangeability for other biologics for the same condition of use for the lesser of (i) one year after first commercial marketing of the first interchangeable biosimilar, (ii) eighteen months after the first interchangeable biosimilar is approved if there is no patent challenge, (iii) eighteen months after resolution of a lawsuit over the patents of the reference biologic in favor of the first interchangeable biosimilar applicant, or (iv) 42 months after the first interchangeable biosimilar's application has been approved if a patent lawsuit is ongoing within the 42-month period.

### *Disclosure of clinical trial information*

Sponsors of clinical trials of FDA-regulated products, including drugs, are required to register and disclose certain clinical trial information. Information related to the product, patient population, phase of investigation, trial sites and investigators, and other aspects of the clinical trial is then made public as part of the registration. Sponsors are also obligated to discuss the results of their clinical trials after completion. Disclosure of the results of these trials can be delayed until the new product or new indication being studied has been approved. Competitors may use this publicly available information to gain knowledge regarding the progress of development programs.



### **European Union—EMA process**

In the European Union, medicinal products are authorized following a similar demanding process as that required in the United States and applications are based on the ICH Common Technical Document. Prior to submitting a European Marketing Authorization Application, or MAA, it is necessary to gain approval of a detailed Pediatric Investigation Plan, or PIP, with the European Medicines Agency's Pediatric Committee, or PDCO. After gaining PIP approval, medicines can be authorized in the European Union by using either the centralized authorization procedure or national authorization procedures.

#### *Centralized procedure*

Under the centralized procedure, after the EMA issues an opinion, the European Commission issues a single marketing authorization valid across the European Union, as well as Iceland, Liechtenstein and Norway. The centralized procedure is compulsory for human medicines that are: derived from biotechnology processes, such as genetic engineering; contain a new active substance indicated for the treatment of certain diseases, such as HIV/AIDS, cancer, diabetes, neurodegenerative disorders or autoimmune diseases and other immune dysfunctions; and officially designated orphan medicines. For medicines that do not fall within these categories, an applicant has the option of submitting an application for a centralized marketing authorization to the EMA, as long as the medicine concerned is a significant therapeutic, scientific or technical innovation, or if its authorization would be in the interest of public health.

#### *National authorization procedures*

There are also two other possible routes to authorize medicinal products in several countries, which are available for products that fall outside the scope of the centralized procedure:

- *Decentralized procedure.* Using the decentralized procedure, an applicant may apply for simultaneous authorization in more than one European Union country of a medicinal product that has not yet been authorized in any European Union country and that does not fall within the mandatory scope of the centralized procedure.
- *Mutual recognition procedure.* In the mutual recognition procedure, a medicine is first authorized in one European Union Member State, in accordance with the national procedures of that country. Thereafter, further marketing authorizations can be sought from other European Union countries in a procedure whereby the countries concerned agree to recognize the validity of the original, national marketing authorization.

While we believe that our development program, proposed Phase 3 trial design, and overall non-clinical and clinical data package could support future regulatory approval of PRT-201 in the European Union, we have not submitted such information to the European Union for their review.

#### *Good manufacturing practices*

Like the FDA, the EMA, the competent authorities of the European Union Member States and other regulatory agencies regulate and inspect equipment, facilities and processes used in the manufacturing of pharmaceutical and biologic products prior to approving a product. If, after receiving clearance from regulatory agencies, a company makes a material change in manufacturing equipment, location, or process, additional regulatory review and approval may be required. Once we or our partners commercialize products, we will be required to comply with cGMP, and product-specific regulations enforced by, the European Commission, the EMA and the competent authorities of European Union Member States following product approval. Also like the FDA, the EMA, the competent authorities of the European Union Member States and other regulatory agencies also conduct regular, periodic visits to re-inspect equipment, facilities, and processes following the initial approval of a product. If, as a result of these inspections, it is determined that our or our partners' equipment, facilities, or processes do not comply

with applicable regulations and conditions of product approval, regulatory agencies may seek civil, criminal or administrative sanctions and/or remedies against us, including the suspension of our manufacturing operations or the withdrawal of our product from the market.

#### *Data and market exclusivity*

Similar to the United States, there is a process for authorization of generic versions of innovator drug products in the European Union. Abridged applications for the authorization of generic versions of drugs authorized by EMA can be submitted to the EMA through a centralized procedure referencing the innovator's data and demonstrating bioequivalence to the reference product, among other things.

New medicinal products in the European Union can receive eight years of data exclusivity coupled with two years of market exclusivity, and a potential one year extension, if the marketing authorizations holder obtains an authorization for one or more new therapeutic indications that demonstrates "significant clinical benefit" in comparison with existing therapies; this system is usually referred to as "8+2+1". We expect to be eligible for at least ten years of market exclusivity following any approval of PRT-201.

Abridged applications cannot rely on an innovator's data until after expiry of the eight year data exclusivity term; applications for a generic product can be filed but the product cannot be marketed until the end of the market exclusivity term.

#### ***Other international markets—drug approval process***

In some international markets (*e.g.*, China or Japan), although data generated in United States or European Union trials may be submitted in support of a marketing authorization application, additional clinical trials conducted in the host territory, or studying people of the ethnicity of the host territory, may be required prior to the filing or approval of marketing applications within the country.

#### ***Pricing and reimbursement***

In the United States and internationally, sales of products that we market in the future, and our ability to generate revenues on such sales, are dependent, in significant part, on the availability and level of reimbursement from third-party payors such as state and federal governments, managed care providers and private insurance plans. Substantial uncertainty exists as to the reimbursement status of newly approved healthcare products by third-party payors. In the United States no uniform policy of coverage and reimbursement for drug products exists. Accordingly, decisions regarding the extent of coverage and amount of reimbursement to be provided for any of our products will be made on a payor by payor basis. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our product candidates to each payor separately, with no assurance that coverage and adequate reimbursement will be obtained.

Private insurers, such as health maintenance organizations and managed care providers, have implemented cost-cutting and reimbursement initiatives and likely will continue to do so in the future. These include establishing formularies that govern the drugs and biologics that will be offered and also the out-of-pocket obligations of member patients for such products. In addition, particularly in the United States and increasingly in other countries, we may be required to provide discounts and pay rebates to state and federal governments and agencies in connection with purchases of our products that are reimbursed by such entities. It is possible that future legislation in the United States and other jurisdictions could be enacted which could potentially impact the reimbursement rates for the products we are developing and may develop in the future and also could further impact the levels of discounts and rebates paid to federal and state government entities. Any legislation that impacts these areas could impact, in a significant way, our ability to generate revenues from sales of products that, if successfully developed, we bring to market.

There is no legislation at the European Union level governing the pricing and reimbursement of medicinal products in the European Union. As a result, the competent authorities of each of the 27 European Union Member States have adopted individual strategies regulating the pricing and reimbursement of medicinal products in their territory. These strategies often vary widely in nature, scope and application. However, a major element that they have in common is an increased move towards reduction in the reimbursement price of medicinal products, a reduction in the number and type of products selected for reimbursement and an increased preference for generic products over innovative products. These efforts have mostly been executed through these countries' existing price control methodologies. The government of the UK announced the phase-out of its established Pharmaceutical Pricing Reimbursement Scheme approach in January 2014 and the adoption of a new value-based pricing approach. Under this approach, in a complete departure from established methodologies, reimbursement levels of each drug will be explicitly based on an assessment of value, looking at the benefits for the patient, unmet need, therapeutic innovation, and benefit to society as a whole. It is increasingly common in many European Union Member States for Marketing Authorization Holders to be required to demonstrate the pharmaco-economic superiority of their products as compared to products already subject to pricing and reimbursement in specific countries. In order for drugs to be evaluated positively under such criteria, pharmaceutical companies may need to re-examine, and consider altering, a number of traditional functions relating to the selection, study, and management of drugs, whether currently marketed, under development, or being evaluated as candidates for research and/or development.

### ***Sales and marketing***

Sales, promotion and other activities following product approval are subject to regulation by numerous regulatory authorities in addition to the FDA, including, in the United States, the Centers for Medicare & Medicaid Services, other divisions of the Department of Health and Human Services, the U.S. Department of Justice, and similar foreign, state, and local government authorities.

As described above, the FDA regulates all advertising and promotion activities for products under its jurisdiction both prior to and after approval. A company can make only those claims relating to safety and efficacy that are approved by the FDA in labeling. Physicians may prescribe legally available drugs for uses that are not described in the drug's labeling and that differ from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties, and often reflect a physician's belief that the off-label use is the best treatment for the patients. The FDA does not regulate the behavior of physicians in their choice of treatments, but FDA regulations do impose stringent restrictions on manufacturers' communications regarding off-label uses. Failure to comply with applicable FDA requirements may subject a company to adverse publicity, enforcement action by the FDA, corrective advertising, consent decrees and the full range of civil and criminal penalties available to the FDA.

In the United States sales, marketing and scientific/educational programs must also comply with various federal and state laws pertaining to healthcare "fraud and abuse," including anti-kickback laws and false claims laws. Anti-kickback laws make it illegal for a prescription drug manufacturer to solicit, offer, receive, or pay any remuneration in exchange for, or to induce, the referral of business, including the purchase or prescription of a particular drug. Due to the breadth of the statutory provisions and the absence of guidance in the form of regulations and very few court decisions addressing industry practices, it is possible that our practices might be challenged under anti-kickback or similar laws. Moreover, recent healthcare reform legislation has strengthened these laws. For example, the recently enacted Patient Protection and Affordable Care Act, or PPACA, among other things, amends the intent requirement of the federal anti-kickback and criminal healthcare fraud statutes to clarify that a person or entity does not need to have actual knowledge of this statute or specific intent to violate it. In addition, PPACA clarifies that the government may assert that a claim that includes items or services resulting from a violation of the federal anti-kickback statute constitutes a false or fraudulent claim for purposes of the false claims statutes to clarify that. False claims laws prohibit anyone from knowingly and willingly presenting, or causing to be

presented for payment, to third-party payors (including Medicare and Medicaid) claims for reimbursed drugs or services that are false or fraudulent, claims for items or services not provided as claimed, or claims for medically unnecessary items or services. Our activities relating to the sale and marketing of our products may be subject to scrutiny under these laws. Violations of fraud and abuse laws may be punishable by criminal and civil sanctions, including fines and civil monetary penalties, the possibility of exclusion from federal healthcare programs (including Medicare and Medicaid) and corporate integrity agreements, which impose, among other things, rigorous operational and monitoring requirements on companies. Similar sanctions and penalties also can be imposed upon executive officers and employees, including criminal sanctions against executive officers under the so-called "responsible corporate officer" doctrine, even in situations where the executive officer did not intend to violate the law and was unaware of any wrongdoing.

Given the significant penalties and fines that can be imposed on companies and individuals if convicted, allegations of such violations often result in settlements even if the company or individual being investigated admits no wrongdoing. Settlements often include significant civil sanctions, including fines and civil monetary penalties, and corporate integrity agreements. If the government were to allege or convict us or our executive officers of violating these laws, our business could be harmed. In addition, private individuals have the ability to bring similar actions. Our activities could be subject to challenge for the reasons discussed above and due to the broad scope of these laws and the increasing attention being given to them by law enforcement authorities. Further, there are an increasing number of state laws that require manufacturers to make reports to states on pricing and marketing information. Many of these laws contain ambiguities as to what is required to comply with the laws. Given the lack of clarity in laws and their implementation, our reporting actions could be subject to the penalty provisions of the pertinent state authorities.

Similar rigid restrictions are imposed on the promotion and marketing of medicinal products in the European Union and other countries. Laws (including those governing promotion, marketing and anti-kickback provisions), industry regulations and professional codes of conduct often are strictly enforced. Even in those countries where we are not directly responsible for the promotion and marketing of our products, inappropriate activity by our international distribution partners can have adverse implications for us.

#### ***Other laws and regulatory processes***

We will become subject to a variety of financial disclosure and securities trading regulations as a public company in the United States, including laws relating to the oversight activities of the SEC and, following the listing of our capital stock on the NASDAQ Global Market, we will be subject to the regulations of the NASDAQ Global Market. In addition, the Financial Accounting Standards Board, or FASB, the SEC and other bodies that have jurisdiction over the form and content of our accounts, our financial statements and other public disclosure are constantly discussing and interpreting proposals and existing pronouncements designed to ensure that companies best display relevant and transparent information relating to their respective businesses.

Our international operations are subject to compliance with the Foreign Corrupt Practices Act, or the FCPA, which prohibits corporations and individuals from paying, offering to pay, or authorizing the payment of anything of value to any foreign government official, government staff member, political party, or political candidate in an attempt to obtain or retain business or to otherwise influence a person working in an official capacity. We also may be implicated under the FCPA for activities by our partners, collaborators, CROs, vendors or other agents.

Our present and future business has been and will continue to be subject to various other laws and regulations. Various laws, regulations and recommendations relating to safe working conditions, laboratory practices, the experimental use of animals, and the purchase, storage, movement, import and export and

use and disposal of hazardous or potentially hazardous substances used in connection with our research work are or may be applicable to our activities. Certain agreements entered into by us involving exclusive license rights or acquisitions may be subject to national or supranational antitrust regulatory control, the effect of which cannot be predicted. The extent of government regulation, which might result from future legislation or administrative action, cannot accurately be predicted.

### **Legal Proceedings**

We are not currently a party to any material legal proceedings.

### **Facilities**

Our primary facility is located in Waltham, Massachusetts, where we occupy approximately 4,943 square feet of office space. Our lease expires in December 2014. We also have facility located in Kansas City, Kansas, where we occupy approximately 250 square feet of office space. Our lease in Kansas City expires in December 2014. We are currently reviewing options with respect to our primary facility in Waltham, Massachusetts upon expiration of our current lease, including re-letting our current facility or re-locating our primary facility to another location in the greater Boston, Massachusetts metropolitan area. We believe that suitable space will be available on commercially reasonable terms.

### **Employees**

As of May 31, 2014, we had 11 full-time employees and one part-time employee, including seven in research and development and five in general and administrative functions. None of our employees is subject to a collective bargaining agreement or represented by a labor or trade union. We believe that our relations with our employees are good.

**MANAGEMENT****Executive Officers and Directors**

The following table sets forth the names, ages and positions of the directors and executive officers of Proteon as of June 24, 2014:

<b>Name</b>	<b>Age</b>	<b>Position(s)</b>
Timothy P. Noyes	52	President, Chief Executive Officer and Director
Steven K. Burke, M.D.	53	Senior Vice President and Chief Medical Officer
George A. Eldridge	51	Senior Vice President, Chief Financial Officer, Treasurer and Secretary
Daniel P. Gottlieb	44	Vice President, Marketing and Business Development
<b>Non-Employee Directors</b>		
Hubert Birner, Ph.D.(1)(2)(3)	48	Director
Todd Foley(2)(3)	42	Director
F. Nicholas Franano, M.D.	47	Director
John G. Freund, M.D.	60	Director
Tim Haines(1)(3)	56	Director
Dmitry Kobyzev(2)(3)	29	Director
Brendan M. O'Leary, Ph.D.(1)(2)	42	Director
Gregory D. Phelps(1)	65	Chairman of the Board of Directors

- (1) Member of the Compensation Committee.
- (2) Member of the Audit Committee.
- (3) Member of the Nominating and Corporate Governance Committee.

**Executive Officers**

**Timothy P. Noyes** joined Proteon in April 2006 as our President and Chief Executive Officer and has also been a member of our board of directors since joining Proteon. From 2002 to 2006, Mr. Noyes served as Chief Operating Officer of Trine Pharmaceuticals, Inc. Before joining Trine, Mr. Noyes held several management positions with GelTex Pharmaceuticals from 1996 to 2001, prior to its acquisition by Genzyme Corporation. After the acquisition, from 2001 to 2002, he held the positions of President, Renal Division and President, GelTex Pharmaceuticals. Prior to GelTex, he worked for several years at Merck & Co. across multiple roles in its hypertension and heart failure group and managed care division, and on its Vasotec and Prilosec products. Mr. Noyes received an A.B. from Harvard College and an M.B.A. from Harvard Business School. We believe Mr. Noyes is qualified to serve as a member of our board of directors because of his role with us and his extensive operational knowledge of, and executive level management experience in, the biopharmaceutical industry.

**Steven K. Burke, M.D.**, joined Proteon in August 2006 as our Senior Vice President and Chief Medical Officer. Prior to joining Proteon, Dr. Burke held various roles at Genzyme Corporation from 2000 to 2006, where he served most recently as Senior Vice President of Medical and Regulatory Affairs and Vice President of Clinical Research. From 1994 to 2000, Dr. Burke held roles at GelTex Pharmaceuticals, including Vice President of Clinical Research and Medical Director, and before that he held positions at Glaxo. Dr. Burke received an A.B. from Harvard College and an M.D. from Cornell University Medical College. He completed a medical residency and fellowship at Brigham and Women's Hospital and is certified by the American Board of Internal Medicine.

**George A. Eldridge** joined Proteon in September 2013 as our Senior Vice President and Chief Financial Officer. Prior to joining Proteon, from 2009 to 2013, Mr. Eldridge served as a consultant to companies in the biotechnology industry, acting as a chief financial officer and providing advisory services. From 2006 to 2009, Mr. Eldridge was Chief Financial Officer of Targanta Therapeutics Corporation until its acquisition in 2009 by The Medicines Company. Before working at Targanta, Mr. Eldridge served as Chief Financial Officer of Therion Biologics from 2002 to 2006. In the fourth quarter of 2006, Therion filed a petition under the federal bankruptcy laws, which was rejected. Prior to Therion Mr. Eldridge served as Chief Financial Officer of Curis, Inc. (previously Ontogeny, Inc.) and Boston Life Sciences, Inc. Prior to working in the biotechnology field, Mr. Eldridge was an investment banker at Kidder Peabody & Co, Inc.. He holds a B.A. from Dartmouth College and an M.B.A. from the University of Chicago, Booth School of Business.

**Daniel P. Gottlieb** joined Proteon in September 2007 and has served as our Vice President, Marketing and Business Development since March 2013, prior to which he was the Senior Director of Marketing and Business Development from June 2010 until March 2013 and Director of Marketing and Business Development from 2007 until 2010. Prior to joining Proteon, Mr. Gottlieb served as Strategic Marketing Manager of Endovascular Products at Abbott Vascular from 2006 to 2007. Prior to that, Mr. Gottlieb spent seven years, from 1999 to 2006, at Guidant Corporation in a variety of roles, including marketing and market research, strategic planning, and business development and corporate venture investing as part of Guidant's Compass Group. Mr. Gottlieb holds a B.A. from the University of Pennsylvania and an M.B.A. from the Tuck School of Business at Dartmouth College.

#### **Non-Employee Directors**

**Hubert Birner, Ph.D.**, has served as a member of our board of directors since 2007. Dr. Birner is the managing partner of TVM Capital, a venture capital firm, which he joined in 2000. Before joining TVM Capital, Dr. Birner served as Head of Business Development Europe and Director of Marketing for Germany at Zeneca from 1998 to 2000. Dr. Birner joined Zeneca from McKinsey & Company's European Health Care and Pharmaceutical practice where he worked from 1995 to 1998. From 1992 to 1994, Dr. Birner was also an Assistant Professor for biochemistry at the Ludwig-Maximilian-University in Munich. Dr. Birner currently serves as Chairman of the Board of Argos Therapeutics Inc. and Spopharm Holding BV and he previously served as a member of the board of directors of Horizon Pharma, Evotec AG, and BioXcell SPA. Dr. Birner received an M.B.A. from Harvard Business School and a Ph.D. in biochemistry from Ludwig-Maximilian-University Munich, where he graduated summa cum laude. We believe Dr. Birner is qualified to serve as a member of our board of directors because of his business and professional experience.

**Todd Foley** has served as a member of our board of directors since May 2012. Mr. Foley is a managing director with MPM Capital, a venture capital firm, which he joined in 1999. Prior to joining MPM, Mr. Foley worked in business development at Genentech in 1998 and in management consulting with Arthur D. Little from 1994 to 1997. Mr. Foley currently serves as a member of the board of directors of Aires Pharmaceuticals, Inc., Celladon Corporation, Chiasma, Inc. and Selexys Pharmaceuticals Corporation and he previously served as a member of the board of directors of Zalicus Inc. Mr. Foley received a B.S. in chemistry from the Massachusetts Institute of Technology and an M.B.A. from Harvard Business School. We believe Mr. Foley is qualified to serve as a member of our board of directors because of his business and professional experience.

**F. Nicholas Franano, M.D.**, has served as a member of our board of directors since March 2006. Dr. Franano is currently President and Chief Executive Officer of Flow Forward Medical, Inc., and Metactive Medical, Inc., two companies developing cardiovascular medical devices that may compete with our products, where he has served since January 2014. Prior to this, Dr. Franano was founder, President and Chief Executive Officer of Novita Therapeutics, a medical device incubator company, from 2009 to 2013. Dr. Franano founded Proteon, and served as our Chief Executive Officer from 2001 to 2006, and, after that, as our Chief Scientific Officer from 2006 to 2009. Dr. Franano received an M.D. and an M.A. in

biomedical research from Washington University, St. Louis, and a B.S. in cell biology from the University of Kansas. He completed a residency in diagnostic radiology and a fellowship in interventional radiology at the Johns Hopkins Hospital. Prior to founding Proteon, Dr. Franano maintained a clinical practice in interventional radiology from 2000 through 2005. We believe Dr. Franano is qualified to serve as a member of our board of directors because of his business and professional experience.

**John G. Freund, M.D.**, became a member of our board of directors in February 2014. Dr. Freund co-founded Skyline Ventures, a venture capital firm, in September 1997, where he has served as a partner since its founding. Prior to joining Skyline, Dr. Freund served as managing director in the private equity group of Chancellor Capital Management from 1995 to 1997. In 1995, he co-founded Intuitive Surgical, Inc. and served on its board of directors until 2000. From 1988 to 1994, Dr. Freund served in various positions at Acuson Corporation, now part of Siemens, most recently as Executive Vice President. Prior to joining Acuson, Dr. Freund was a general partner of Morgan Stanley Venture Partners from 1987 to 1988. From 1982 to 1988, Dr. Freund worked at Morgan Stanley & Co., where he co-founded the Healthcare Group in the Corporate Finance Department. Dr. Freund currently serves as a member of the board of directors of the following public companies: XenoPort, Inc., Tetrphase Pharmaceuticals, Inc. and Concert Pharmaceuticals, Inc. He was on the board of MAKO Surgical Corp. from 2008 until its acquisition in 2013. Dr. Freund also serves as a member of the board of directors of the following private companies: Advion, Inc., Collegium Pharmaceuticals, Inc., DiscoverRx Corporation, SI Bone, Inc. and Sutro Biopharma, Inc. He is a director of three mutual funds managed by Capital Research and Management. He is a member of the Advisory Board for the Harvard Business School Healthcare Initiative and is a member of the Therapeutics Advisory Council of Harvard Medical School. He received an A.B. in history from Harvard College, an M.D. from Harvard Medical School and an M.B.A. from Harvard Business School, where he was a Baker Scholar and won the Loeb Fellowship in Finance. We believe Dr. Freund is qualified to serve as a member of our board of directors because of his business and professional experience.

**Tim Haines** became a member of our board of directors in May 2014. Mr. Haines joined Abingworth in 2005 and is currently a partner. From 2000 to 2005, he was Chief Executive of Astex Therapeutics, an Abingworth portfolio company. From 1993 to 2000, Mr. Haines was Chief Executive of two divisions of the publicly-listed medical technology company, Datascope Corp. Prior to Datascope, he held a number of other senior management positions in the US and Europe, including CEO of Thackray Inc and General Manager Baxter UK. Current and past board positions include Astex Pharmaceuticals, Chroma, Fovea, Pixium Vision, PowderMed, Kspine, Stanmore Implants, Lombard Medical, Sientra, and XCounter. Mr. Haines received a B.Sc. from Exeter University and an M.B.A. from INSEAD. We believe Mr. Haines is qualified to serve as a member of our board of directors because of his business and professional experience.

**Dmitry Kobzyev, Ph.D.**, became a member of our board of directors in May 2014. Dr. Kobzyev joined Inbio Ventures, a venture capital management company representing Pharmstandard International S.A., in 2014 and is an Investment Manager. From 2009 to 2014, he served as an Investment Manager of one of the top Russian life science venture capital teams at OJSC RUSNANO. From 2007 to 2009, Dr. Kobzyev advised international private equity and Russian corporate clients within the transactions practice at PricewaterhouseCoopers Russia. Dr. Kobzyev received a Ph.D. degree in economics from Moscow State University. We believe Dr. Kobzyev is qualified to serve as a member of our board of directors because of his business and professional experience.

**Brendan M. O'Leary, Ph.D.**, has been a member of our board of directors since March 2006. Dr. O'Leary joined Prism VentureWorks, a venture capital firm, in 2003 and is currently a general partner. Dr. O'Leary began his professional career with numerous operating roles at IGEN International, a medical diagnostics company (acquired by Roche), where he served from 1999 to 2003, and Meso Scale Discovery, a high-throughput drug discovery start-up, where he served from 1999 to 2003. Dr. O'Leary previously served on the board of directors of Trius Therapeutics. Dr. O'Leary received a Ph.D. in organic chemistry



from the Massachusetts Institute of Technology and a B.A. in chemistry and economics from Middlebury College, and was a Kauffman Fellow. We believe Dr. O'Leary is qualified to serve as a member of our board of directors because of his business and professional experience.

**Gregory D. Phelps** has been a member of our board of directors since February 2008 and has served as Chairman of the Board since July 2009. Mr. Phelps is an independent advisor to biotechnology and pharmaceutical companies. He was a founder and Partner of Red Sky Partners LLC, an advisory firm providing corporate development, product strategy and leadership support to life sciences companies, from February 2009 to February 2014. Prior to that, Mr. Phelps served as Chairman and Chief Executive Officer of RenaMed Biologics, Inc. from 2004 to 2007. Prior to that, he served as Chief Executive Officer of Ardais Corporation from 2002 to 2003, as Vice Chairman and member of the executive committee of Dyax Corporation from 1998 to 2002, as Executive Vice President and Senior Vice President of Genzyme Corporation from 1991 to 1997. Mr. Phelps has previously served as a member of the board of directors of the following companies: EPIX Pharmaceuticals Inc. from 2004 to 2009, Ostex International Inc. from 1995 to 2001, Atlantic Biopharmaceuticals (now Merrimack Pharmaceuticals Inc.) from 1998 to 2000, Neozyme II Corporation from 1992 to 1996, and Genzyme Transgenics Corporation (now rEVO Biologics Inc.) from 1993 to 1995. Mr. Phelps received a B.S. in electrical engineering from Bradley University and an M.B.A. from Harvard Business School. We believe Mr. Phelps is qualified to serve as a member of our board of directors because of his business and professional experience.

### **Composition of the Board of Directors after this Offering**

Our board of directors currently consists of nine members. Our board of directors has determined that each of our Board members except Mr. Noyes is independent for NASDAQ purposes. The members of our board of directors were elected in compliance with the provisions of the voting agreement among us and our major stockholders. The voting agreement will be terminated upon the closing of this offering, and at present we do not have any contractual obligations regarding the election of our directors. See "Certain Relationships and Related Party Transactions." Our directors hold office until their successors have been elected and qualified or until their earlier death, resignation or removal. There are no family relationships among any of our directors or executive officers.

### **Board Committees**

Our board of directors has three standing committees: an audit committee, a compensation committee and a nominating and governance committee. The initial composition and responsibilities of each committee are described below.

#### ***Audit Committee***

Our audit committee is composed of Todd Foley, Hubert Birner, Dmitry Kobzyev and Brendan O'Leary, with \_\_\_\_\_ serving as chairman of the committee. Our board of directors has determined that each of \_\_\_\_\_ satisfies the NASDAQ Stock Market independence standards and the independence standards of Rule 10A-3(b)(1) of the Securities Exchange Act. Our board of directors has determined that \_\_\_\_\_ is an "audit committee financial expert" under applicable rules and regulations of the SEC and the NASDAQ Stock Market.

Our audit committee will provide oversight of our accounting and financial reporting process, the audit of our financial statements and our internal control function. Among other things, our audit committee will be responsible for the following:

- appointing, approving the compensation of, and assessing the qualifications, performance and independence of our independent registered public accounting firm;
- pre-approving audit and permissible non-audit services, and the terms of such services, to be provided by our independent registered public accounting firm;

- reviewing the internal audit plan with the independent registered public accounting firm and members of management responsible for preparing our financial statements;
- reviewing and discussing with management and the independent registered public accounting firm our annual and quarterly financial statements and related disclosures as well as critical accounting policies and practices used by us;
- reviewing the adequacy of our internal control over financial reporting;
- establishing policies and procedures for the receipt and retention of accounting-related complaints and concerns;
- recommending, based upon the audit committee's review and discussions with management and the independent registered public accounting firm, whether our audited financial statements shall be included in our Annual Report on Form 10-K;
- monitoring our compliance with legal and regulatory requirements as they relate to our financial statements and accounting matters;
- preparing the audit committee report required by the rules of the SEC to be included in our annual proxy statement;
- viewing all related party transactions for potential conflict of interest situations and approving all such transactions; and
- reviewing and discussing with management and our independent registered public accounting firm our earnings releases and scripts.

#### ***Compensation Committee***

The members of our compensation committee are Hubert Birner, Tim Haines, Brendan O'Leary and Gregory Phelps, with Brendan O'Leary serving as chairman of the committee. Our board of directors has determined that each of \_\_\_\_\_ satisfies the NASDAQ Stock Market independence standards. Among other things, our compensation committee will be responsible for the following:

- annually reviewing and approving corporate goals and objectives relevant to the compensation of our Chief Executive Officer;
- evaluating the performance of our Chief Executive Officer in light of such corporate goals and objectives and determining and approving the compensation of our Chief Executive Officer;
- reviewing and approving the compensation of our other executive officers;
- appointing, compensating and overseeing the work of any compensation consultant, legal counsel or other advisor retained by the compensation committee;
- conducting the independence assessment outlined in NASDAQ rules with respect to any compensation consultant, legal counsel or other advisor retained by the compensation committee;
- annually reviewing and reassessing the adequacy of the committee charter in its compliance with the listing requirements of NASDAQ;
- reviewing and establishing our overall management compensation, philosophy and policy;
- overseeing and administering our equity compensation and other compensatory plans;
- reviewing and approving our equity and incentive policies and procedures for the grant of equity-based awards and approving the grant of such equity-based awards;
- reviewing and making recommendations to the board of directors with respect to director compensation; and
- reviewing and discussing with management the compensation discussion and analysis to be included in our annual proxy statement or Annual Report on Form 10-K.

#### ***Governance and Nominating Committee***

Our governance and nominating committee is composed of Hubert Birner, Dmitry Kobzyev, Todd Foley and Tim Haines with Hubert Birner serving as chair of the committee. Our board of directors has

determined that each of \_\_\_\_\_ satisfies the NASDAQ Stock Market independence standards.

Our governance and nominating committee will be responsible for, among other things, making recommendations regarding corporate governance, the composition of our board of directors, identification, evaluation and nomination of director candidates and the structure and composition of committees of our board of directors. In addition, our governance and nominating committee will:

- oversee our corporate governance guidelines;
- approve our committee charters;
- oversee compliance with our code of business conduct and ethics;
- contribute to succession planning;
- review actual and potential conflicts of interest of our directors and officers other than related party transactions reviewed by the related-party matters committee; and
- oversee the board self-evaluation process.

#### **Compensation Committee Interlocks and Insider Participation**

None of the members of our compensation committee is or has at any time during the past year been one of our officers or employees. None of our executive officers currently serves, or in the past year has served, as a member of the board of directors or compensation committee of any entity that has one or more executive officers serving on our board of directors or compensation committee.

#### **Code of Business Conduct and Ethics**

We plan to adopt a code of business conduct and ethics that will apply to all of our employees, including our officers and directors, and those employees responsible for financial reporting. The code of business conduct and ethics will be available on our website. We expect that, to the extent required by law, any amendments to the code, or any waivers of its requirements, will be disclosed on our website.

**EXECUTIVE AND DIRECTOR COMPENSATION****Summary Compensation Table**

The following table presents compensation awarded in 2013 to our principal executive officer and our two other most highly compensated persons serving as executive officers as of December 31, 2013 or paid to or accrued for those executive officers for services rendered during 2013. We refer to these executive officers as our "named executive officers."

<u>Name &amp; Principal Position</u>	<u>Year</u>	<u>Salary (\$)</u>	<u>Bonus (\$ (1)</u>	<u>Option Awards (\$)(2)</u>	<u>All Other Compensation (\$)(3)</u>	<u>Total (\$)</u>
Timothy P. Noyes <i>President and Chief Executive Officer</i>	2013	393,710	73,830	—	4,595	472,135
Steven K. Burke, M.D. <i>Senior Vice President and Chief Medical Officer</i>	2013	359,870	80,980	—	5,624	446,474
Daniel Gottlieb <i>Vice President, Marketing and Business Development</i>	2013	203,772	38,630	10,364	1,867	254,633

- (1) Amounts represent cash bonuses earned in 2013, and paid during 2014, based on achievement of performance goals and other factors deemed relevant by our board of directors. Our 2013 company objectives related primarily to development and strategic achievements.
- (2) The amounts reported in the Option Awards column granted to our named executive officers represent the retrospective fair value of the stock options as of the grant date as computed in accordance with Accounting Standards Codification, or ASC, Topic 718, not including any estimates of forfeitures. The assumptions used in calculating the grant date fair value of the stock options reported in the option awards column are set forth in Note 11 to our financial statements included elsewhere in this prospectus. Note that the amounts reported in this column reflect the accounting cost for these stock options, and do not correspond to the actual economic value that may be received by the named executive officers from the options.
- (3) This column reflects term life and disability insurance premiums paid by us on behalf of the named executive officers. All of these benefits are provided to the named executive officers on the same terms as provided to all of our regular full-time employees.

**Executive Compensation****Overview**

Our executive compensation program is based on a pay-for-performance philosophy. We designed our executive compensation program to achieve the following primary objectives: provide compensation and benefit levels that will attract, retain, motivate and reward a highly talented executive team within the context of responsible cost management; establish a direct link between our individual/team performance and results and our executives' compensation; and align the interests and objectives of our executives with those of our stockholders by linking executive equity awards to stockholder value creation. Compensation for our executive officers is composed primarily of the following three main components: base salary; annual cash incentive bonuses and long-term equity incentives.

### **Base Salary**

Base salaries are determined on a case-by-case basis for each named executive officer, including consideration of each officer's experience, expertise and performance, as well as market compensation levels for similar positions.

<u>Name</u>	<u>2013 Base Salary (\$)</u>	<u>2014 Base Salary (\$)</u>
Timothy P. Noyes	393,710	401,590
Steven Burke	359,870	367,070
Daniel P. Gottlieb	206,000	210,120

The 2013 base salary for Mr. Gottlieb became effective in connection with a promotion effective March 1, 2013. The 2013 base salary for Mr. Noyes and Dr. Burke became effective January 1, 2013. The 2014 base salary for each named executive officer became effective January 1, 2014.

### **Annual Cash Incentive Bonuses**

Annual cash incentive bonuses are contingent upon our achievement of certain operational and financial objectives, which for 2013 consisted primarily of research and development goals. Each named executive officer's target bonus amount is expressed as a percentage of the officer's base salary and is intended to be commensurate with the officer's position and responsibilities. Target bonuses for each officer were 25% of base salary for the year ended December 31, 2013.

### **Long-term Equity Incentives**

We believe equity awards in the form of options to purchase shares of our common stock provide an incentive for our named executive officers to focus on driving growth in our stock price and long-term value creation and help us to attract and retain key talent. In addition, the granting of options helps ensure that the interests of our officers are aligned with those of our stockholders as the options only have value if the value of our common stock increases after the date the option is granted.

Our officers are entitled to certain benefits if the officer's employment terminates in certain circumstances or if a change of control occurs. We also may provide our officers with relocation, housing or other benefits in certain circumstances. However, we do not provide any of our officers with a tax gross-up payment on any severance or change-of-control benefits (although we may provide tax reimbursement payments on relocation and other benefits). Our board of directors reviews (and, after this offering, our compensation committee will review) our officers' overall compensation packages on an annual basis or more frequently as it deems appropriate. From time to time, we may retain independent compensation consultants as we consider appropriate to help identify appropriate peer group companies and to obtain and evaluate current executive compensation data. We did not retain compensation consultants in designing our executive compensation programs for 2013. However, the compensation committee has retained independent compensation consultants for 2014 and beyond.

### **Employment Agreements**

Below are written descriptions of our agreements with each of our named executive officers. In addition to the specifics described below, our named executive officers' employment agreements also provide for grants of stock options as described in more detail in the "Outstanding Equity Awards at Fiscal Year End" table below and the footnotes that follow the table.

#### ***Timothy P. Noyes***

In April 2006, we entered into an employment agreement with Mr. Noyes to serve as our President and Chief Executive Officer. We amended the employment agreement in April 2009. Mr. Noyes's

employment with us is "at-will," and the agreement does not include a specified term. The agreement provides that Mr. Noyes receives an annual base salary, initially established at \$320,000 in 2009, and that he is eligible for an annual incentive bonus, with his target bonus being 25% of his base salary. The board of directors determines his actual bonus amount based on its assessment of Proteon's and his individual performance during the year. The agreement also provides for Mr. Noyes to participate in our benefit programs made available to our employees generally.

Under Mr. Noyes's agreement, if his employment is terminated by us without cause or by reason of constructive termination (as such terms are defined in the agreement), he will be entitled to receive cash severance equal to 12 months of his base salary; reimbursement of his COBRA premiums for up to twelve months; and 50% of any unvested stock options or unvested restricted shares (excluding certain grants) shall vest in full, accelerated to 100% if the termination occurs 30 days prior to or 180 days after a corporate transaction (as defined in the agreement). If a termination of Mr. Noyes's employment without cause (as defined in the agreement) occurs at such time as our business is being discontinued because rendered impracticable by substantial financial losses, lack of funding, dissolution or any reason beyond our control his cash severance would be equal to five months of his base salary and would be paid to him in a lump sum. Mr. Noyes's right to receive these severance benefits is subject to his providing a release of claims in favor of Proteon.

The agreement includes a noncompetition covenant during Mr. Noyes's employment under the agreement and for 12 months thereafter. The agreement provides that we shall indemnify Mr. Noyes against all losses, damages, expenses and claims against him by reason of act or omission in connection with the performance of his duties to the fullest extent permitted by the law.

***Steven K. Burke, M.D.***

In July 2006, we entered into an employment agreement with Dr. Burke to serve as our Senior Vice President and Chief Medical Officer. We amended the employment agreement in April 2009. Dr. Burke's employment with us is "at-will," and the agreement does not include a specified term. The agreement provides that Dr. Burke receives an annual base salary, initially established at \$292,000 in 2009, and that he is eligible for an annual incentive bonus, with his target bonus being 25% of his base salary. The board of directors determines his actual bonus amount based on its assessment of Proteon's and his individual performance during the year. The agreement also provides for Dr. Burke to participate in our benefit programs made available to our employees generally.

Under Dr. Burke's agreement, if his employment is terminated by us without cause or by reason of constructive termination (as these terms are defined in the agreement), he will be entitled to receive cash severance equal to 12 months of his base salary; reimbursement of his COBRA premiums for up to twelve months; and 50% of any unvested stock options or unvested restricted shares (excluding certain grants) shall vest in full, accelerated to 100% if the termination occurs 30 days prior to or 180 days after a corporate transaction (as defined in the agreement). If a termination of Dr. Burke's employment without cause (as defined in the agreement) occurs at such time as our business is being discontinued because rendered impracticable by substantial financial losses, lack of funding, dissolution or any reason beyond our control his cash severance would be equal to four months of his base salary and would be paid to him in a lump sum. Dr. Burke's right to receive these severance benefits is subject to his providing a release of claims in favor of Proteon.

The agreement includes a noncompetition covenant during Dr. Burke's employment under the agreement and for 12 months thereafter. The agreement provides that we shall indemnify Dr. Burke against all losses, damages, expenses and claims against him by reason of act or omission in connection with the performance of his duties to the fullest extent permitted by the law.

**Daniel P. Gottlieb**

In July 2007 we entered into an employment agreement with Mr. Gottlieb to serve as our Director of Business Development. Mr. Gottlieb's employment with us is "at-will," and the agreement does not include a specified term. The agreement provides that Mr. Gottlieb receives an annual base salary, initially established at \$160,000 in 2007, and that he is eligible for an annual incentive bonus, with his initial target bonus being 20% of his base salary. The board of directors will determine his actual bonus amount based on its assessment of Proteon's and his individual performance during the year. The agreement also provides for Mr. Gottlieb to participate in our benefit programs made available to our employees generally.

Under a separate severance agreement, if Mr. Gottlieb's employment is terminated by us without cause or by reason of constructive termination (as such terms are defined in the agreement), he will be entitled to receive cash severance equal to six months of his base salary; reimbursement of his COBRA premiums for up to six months; and 100% of any unvested stock options or unvested restricted shares shall vest in full if the termination occurs 30 days prior to or 365 days after a corporate transaction (as defined in the agreement).

**Outstanding Equity Awards at Fiscal Year End**

The following table sets forth information regarding outstanding equity awards held by our named executive officers as of December 31, 2013.

<u>Name</u>	<u>Notes</u>	<u>Number of Securities Underlying Unexercised Options Exercisable(1)</u>	<u>Number of Securities Underlying Unexercised Options Unexercisable</u>	<u>Option Exercise Price (\$)(2)</u>	<u>Option Expiration Date</u>
Timothy P. Noyes	(3)	1,329,000	—	\$ 0.12	8/1/2016
	(3)	500,000	—	\$ 0.15	9/10/2017
	(3)	886,017	—	\$ 0.20	6/18/2019
	(3)	55,221	—	\$ 0.20	12/15/2019
	(4)	1,355,117	—	\$ 0.08	10/26/2021
Steven K. Burke, M.D.	(3)	482,632	—	\$ 0.12	8/1/2016
	(3)	195,000	—	\$ 0.15	9/10/2017
	(3)	236,443	—	\$ 0.20	6/18/2019
	(4)	919,416	—	\$ 0.08	10/26/2021
Daniel P. Gottlieb	(3)	84,374	—	\$ 0.15	9/10/2017
	(3)	29,442	—	\$ 0.20	6/18/2019
	(4)	60,000	—	\$ 0.08	10/26/2021
	(5)	10,000	—	\$ 1.40	3/25/2023

- (1) All of the outstanding option awards were granted under and subject to the terms of our 2006 Equity Incentive plan, described below under "—Equity Benefit and Stock Plans." Except as otherwise indicated, as of December 31, 2013, each option award is immediately exercisable but is subject to repurchase by us until vested. All vesting is subject to the officer's continuous service with us through the vesting dates and the potential vesting acceleration described above under "—Employment Agreements."
- (2) All of the option awards were granted with a per share exercise price equal to the fair market value of one share of our common stock on the date of grant, as determined in good faith by our board of directors

- (3) These grants are fully vested.
- (4) The unvested shares under this option are scheduled to vest in approximately equal quarterly installments through October 1, 2015.
- (5) The unvested shares under this option are scheduled to vest in approximately equal quarterly installments through January 1, 2017.

## **Employee Benefit and Stock Plans**

### ***2006 Equity Incentive Plan***

We adopted our 2006 Equity Incentive Plan, or 2006 Plan, in March 2006, and stockholders approved the plan in March 2006. We amended the 2006 Plan in 2007. Under the 2006 Plan, we are generally authorized to grant options to purchase shares of our common stock to our employees, directors and consultants. Options under the 2006 Plan are either incentive stock options, within the meaning of Section 422 of the Internal Revenue Code, or nonqualified stock options. All options granted under the 2006 Plan expire no later than ten years from their date of grant.

No new awards will be granted under the 2006 Plan after the consummation of this initial public offering. Our board of directors, or a committee appointed by the board, administers the 2006 Plan. As is customary in incentive plans of this nature, the number of shares subject to outstanding awards under the 2006 Plan and the exercise prices of those awards are subject to adjustment in the event of changes in our capital structure, reorganizations and other extraordinary events. In the event that we are consolidated with, or acquired by, another entity in a merger, consolidation or sale of all or substantially all of our assets, the plan administrator will provide for the outstanding awards either to be assumed by our successor or to terminate on the transaction. If the awards terminate, the plan administrator has discretion to provide for the accelerated vesting of the awards prior to their termination.

Our board of directors may amend or terminate the 2006 Plan at any time, except that any such amendment or termination may not adversely affect the rights of a holder of an outstanding award without the holder's consent. The 2006 Plan requires that certain amendments, to the extent required by applicable law or any applicable listing agency or deemed necessary or advisable by the board of directors, be submitted to stockholders for their approval.

### ***2014 Equity Incentive Plan***

The following is a summary of the material terms of the 2014 Equity Incentive Plan, or 2014 Plan, which will be in effect upon the completion of this offering. It does not purport to be complete and is qualified by reference to the full text of the 2014 Equity Incentive Plan, which we will file as an exhibit to our registration statement of which this prospectus is a part.

The 2014 Plan provides for the grant of incentive stock option and nonstatutory stock options, stock appreciation rights, restricted stock and stock unit awards, performance units, stock grants and qualified performance-based awards, which we collectively refer to as "awards" in connection with the 2014 Plan. Directors, officers and other employees of Proteon and our subsidiaries, as well as others performing consulting or advisory services for us, are eligible for grants under the 2014 Plan. The purpose of the 2014 Plan is to provide incentives that will attract, retain and motivate highly competent officers, directors, employees and consultants to promote the success of our business.

#### *Administration*

Under its terms, the 2014 Plan is administered by the compensation committee of the board of directors. The board of directors itself may also exercise any of the powers and responsibilities under the



2014 Plan. Subject to the terms of the 2014 Plan, the plan administrator (the board or its compensation committee) will select the recipients of awards and determine, among other things, the:

- number of shares of common stock covered by the awards and the dates upon which such awards become exercisable or any restrictions lapse, as applicable;
- type of award and the exercise or purchase price and method of payment for each such award;
- vesting period for awards, risks of forfeiture and any potential acceleration of vesting or lapses in risks of forfeiture; and
- duration of awards.

All decisions, determinations and interpretations by the compensation committee with respect to the 2014 Plan and the terms and conditions of or operation of any award are final and binding on all participants, beneficiaries, heirs, assigns or other persons holding or claiming rights under the 2014 Plan or any award.

#### *Available Shares*

The aggregate number of shares of our common stock which may be issued or used for reference purposes under the 2014 Plan or with respect to which awards may be granted, subject to the automatic increase provisions described below, may not exceed \_\_\_\_\_ shares, which may be either authorized and unissued shares of our common stock or shares of common stock held in or acquired for our treasury. In general, if awards under the 2014 Plan are for any reason cancelled, or expire or terminate unexercised, the number of shares covered by such awards will again be available for the grant of awards under the 2014 Plan. In addition, (i) shares used to pay the exercise price of a stock option and (ii) shares delivered to or withheld by us to pay the withholding taxes related to an award do not count as shares issued under the 2014 Plan.

The number of shares of common stock authorized under the 2014 Equity Incentive Plan also will be increased each January 1 starting in 2015 by an amount equal to the lesser of (i) \_\_\_\_\_ % of our outstanding common stock on a fully diluted basis as of the end of our immediately preceding fiscal year, (ii) \_\_\_\_\_ shares, and (iii) any lower amount determined by our board prior to each such January 1.

#### *Eligibility for Participation*

Members of our board of directors, as well as employees of, and consultants to, us or any of our subsidiaries and affiliates are eligible to receive awards under the 2014 Plan. The selection of participants is within the sole discretion of the compensation committee.

#### *Incentive Stock Options*

Incentive stock options are intended to qualify as incentive stock options under Section 422 of the Internal Revenue Code and will be granted pursuant to incentive stock option agreements. The plan administrator will determine the exercise price for an incentive stock option, which may not be less than 100% of the fair market value of the stock underlying the option determined on the date of grant. In addition, incentive options granted to employees who own, or are deemed to own, more than 10% of our voting stock, must have an exercise price not less than 110% of the fair market value of the stock underlying the option determined on the date of grant.

#### *Nonstatutory Stock Options*

Nonstatutory stock options are not intended to qualify as incentive stock options under Section 422 of the Internal Revenue Code and will be granted pursuant to nonstatutory stock option agreements. The plan administrator will determine the exercise price for a nonstatutory stock option, which may not be less than the fair market value of the stock underlying the option determined on the date of grant.

### *Stock Appreciation Rights*

A stock appreciation right, or a SAR, entitles a participant to receive a payment equal in value to the difference between the fair market value of a share of stock on the date of exercise of the SAR over the grant price of the SAR. SARs may be granted in tandem with a stock option, such that the recipient has the opportunity to exercise either the stock option or the SAR, but not both. The base exercise price (above which any appreciation is measured) will not be less than 50% of the fair market value of the common stock on the date of grant of the SAR or, in the case of an SAR granted in tandem with a stock option, the exercise price of the related stock option. The administrator may pay that amount in cash, in shares of our common stock, or a combination. The terms, methods of exercise, methods of settlement, form of consideration payable in settlement, and any other terms and conditions of any SAR will be determined by the administrator at the time of the grant of award and will be reflected in the award agreement.

### *Restricted Stock and Stock Units*

A restricted stock award or restricted stock unit award is the grant of shares of our common stock either currently (in the case of restricted stock) or at a future date (in the case of restricted stock units) at a price determined by the administrator (including zero), that is nontransferable and is subject to substantial risk of forfeiture until specific conditions or goals are met. Conditions are typically based on continuing employment. During the period of restriction, participants holding shares of restricted stock shall, except as otherwise provided in an individual award agreement, have full voting and dividend rights with respect to such shares. Participants holding restricted stock units may be entitled to receive payments equivalent to any dividends declared with respect to the common stock referenced in the grant of the restricted stock units, but only following the close of the applicable restriction period and then only if the underlying common stock has been earned. The restrictions will lapse in accordance with a schedule or other conditions determined by the administrator.

### *Performance Units*

A performance unit award is a contingent right to receive predetermined shares of our common stock if certain performance goals are met. The value of performance units will depend on the degree to which the specified performance goals are achieved but are generally based on the value of our common stock. The administrator may, in its discretion, pay earned performance shares in cash, or stock, or a combination of both. Furthermore, based on the level of performance, the number of shares issued upon achievement of specified levels of performance could be up to % of the number of performance units.

Our compensation committee has discretion to select the length of any applicable restriction or performance period, the kind and/or level of the applicable performance goal, and whether the performance goal is to apply to us, one of our subsidiaries or any division or business unit, or to the recipient, provided that any performance goals be objective and otherwise meet the requirements of Section 162(m) of the Code. Generally, a recipient will be eligible to receive payment under a qualified performance-based award only if the applicable performance goal or goals are achieved within the applicable performance period, as determined by the compensation committee.

### *Stock Grants*

A stock grant is an award of shares of common stock without restriction. Stock grants may only be made in limited circumstances, such as in lieu of other earned compensation. Stock grants are made without any forfeiture conditions.

### *Qualified Performance-Based Awards*

Qualified performance-based awards include performance criteria intended to satisfy Section 162(m) of the Code. Section 162(m) of the Internal Revenue Code limits our federal income tax deduction for

compensation to certain specified senior executives to \$1 million, but excludes from that limit "performance-based compensation." Any form of award permitted under the 2014 Plan, other than restricted stock, restricted stock units and stock grants, may be granted as a qualified performance-based award, but in each case will be subject to satisfaction of performance goals or (in the case of stock options) based on continued service. The performance criteria used to establish performance goals are limited to the following: (i) cash flow (before or after dividends); (ii) earnings per share (including, without limitation, earnings before interest, taxes, depreciation and amortization); (iii) stock price; (iv) return on equity; (v) stockholder return or total stockholder return; (vi) return on capital (including, without limitation, return on total capital or return on invested capital); (vii) return on investment; (viii) return on assets or net assets; (ix) market capitalization; (x) economic value added; (xi) debt leverage (debt to capital); (xii) revenue; (xiii) sales or net sales; (xiv) backlog; (xv) income, pre-tax income or net income; (xvi) operating income or pre-tax profit; (xvii) operating profit, net operating profit or economic profit; (xviii) gross margin, operating margin or profit margin; (xix) return on operating revenue or return on operating assets; (xx) cash from operations; (xxi) operating ratio; (xxii) operating revenue; (xxiii) market share improvement; (xxiv) general and administrative expenses and (xxv) customer service.

#### *Transferability*

Awards granted under the 2014 Plan are generally nontransferable (other than by will or the laws of descent and distribution), except that the compensation committee may provide for the transferability of nonstatutory stock options at the time of grant or thereafter to certain family members.

#### *Adjustment for Corporate Actions*

In the event of any change in the outstanding shares of common stock as a result of a reorganization, recapitalization, reclassification, stock dividend, stock split, reverse stock split or other similar distribution with respect to the shares of common stock, an appropriate and proportionate adjustment will be made in (i) the maximum numbers and kinds of shares subject to the 2014 Plan, (ii) the numbers and kinds of shares or other securities subject to then outstanding awards, (iii) the exercise price for each share or other unit of any other securities subject to then outstanding stock options or SARs (without change in the aggregate purchase price as to which such stock options or SARs remain exercisable), and (iv) the repurchase price of each share of restricted stock then subject to a risk of forfeiture in the form of a Company repurchase right. Any such adjustment in awards will be determined and made by the Compensation Committee in its sole discretion.

#### *Transactions*

In the event of a transaction, including (i) any merger or consolidation of Proteon, (ii) any sale or exchange of all of the common stock of Proteon, (iii) any sale, transfer or other disposition of all or substantially all of Proteon's assets, or (iv) any liquidation or dissolution of Proteon, the compensation committee may, with respect to all or any outstanding stock options and SARs, (1) provide that such awards will be assumed, or substantially equivalent rights shall be provided in substitution therefore, (2) provide that the recipient's unexercised awards will terminate immediately prior to the consummation of such transaction unless exercised within a specified period following written notice to the recipient, (3) provide that outstanding awards shall become exercisable in whole or in part prior to or upon the transaction, (4) provide for cash payments, net of applicable tax withholdings, to be made to the recipients, (5) provide that, in connection with a liquidation or dissolution of Proteon, awards shall convert into the right to receive liquidation proceeds net of the exercise price of the awards and any applicable tax withholdings, or (6) any combination of the foregoing. With respect to outstanding awards other than stock options or SARs, upon the occurrence of a transaction other than a liquidation or dissolution of the Company which is not part of another form of transaction, the repurchase and other rights of Proteon under each such award will transfer to Proteon's successor. Upon the occurrence of such a liquidation or dissolution of Proteon, all risks of forfeiture and performance goals applicable to such other awards will

automatically be deemed terminated or satisfied, unless specifically provided to the contrary in the award. Any determinations required to carry out any of the foregoing will be made by the compensation committee in its sole discretion.

#### *Change of Control*

Upon the occurrence of a change of control, all outstanding stock options and SARs will accelerate with respect to such percentage of the shares not then exercisable as is determined by the compensation committee, the risk of forfeiture applicable to all outstanding restricted stock and restricted stock units not based on achievement of performance goals will lapse with respect to such percentage of the restricted stock and restricted stock units still subject to such risk of forfeiture as is determined by the compensation committee, and such percentage of any outstanding awards of performance units will be deemed to have been satisfied as is determined by the compensation committee. In each case, a pro rata portion of each unvested award will be vested.

A change of control is defined as the occurrence of any of the following: (1) a transaction, as described above, unless securities possessing more than 50% of the total combined voting power of the resulting entity or ultimate parent entity are held by a person who held securities possessing more than 50% of the total combined voting power of Proteon immediately prior to the transaction; (2) any person or group of persons, excluding Proteon and certain other related entities, directly or indirectly acquires beneficial ownership of securities possessing more than 50% of the total combined voting power of Proteon, unless pursuant to a tender or exchange offer that Proteon's board of directors recommends stockholders accept; (3) over a period of no more than 24 consecutive months there is a change in the composition of Proteon's board such that a majority of the board members ceases to be composed of individuals who either (i) have been board members continuously since the beginning of that period, or (ii) have been elected or nominated for election as board members during such period by at least a majority of the remaining board members who have been board members continuously since the beginning of that period.

#### *Amendment and Termination*

Our board of directors may at any time amend any or all of the provisions of the 2014 Equity Incentive Plan, or suspend or terminate it entirely, retroactively or otherwise. Unless otherwise required by law or specifically provided in the 2014 Equity Incentive Plan, the rights of a participant under awards granted prior to any amendment, suspension or termination may not be adversely affected without the consent of the participant. The 2014 Equity Incentive Plan expires after ten years.

#### *Allocation of Awards; Plan Benefits.*

It is not presently possible to determine the dollar value of award payments that may be made or the number of options, shares of restricted stock, restricted stock units, or other awards that may be granted under the 2014 Equity Incentive Plan in the future, or the individuals who may be selected for such awards because awards under the 2014 Equity Incentive Plan are granted at the discretion of the compensation committee.

#### **401(k) Plan**

We maintain a defined contribution employee retirement plan, or 401(k) plan, for our employees. Our named executive officers are also eligible to participate in the 401(k) plan on the same basis as our other employees. The 401(k) plan is intended to qualify as a tax-qualified plan under Section 401(k) of the Code. The plan provides that each participant may contribute up to the statutory limit, which is \$17,500 for calendar year 2014. Participants that are 50 years or older can also make "catch-up" contributions, which in calendar year 2014 may be up to an additional \$5,500 above the statutory limit. We may also elect to provide for discretionary profit sharing contributions, but we did not provide any such contributions in 2013. In general, eligible compensation for purposes of the 401(k) plan includes an employee's earnings

reportable on IRS Form W-2 subject to certain adjustments and exclusions required under the Code. The 401(k) plan currently does not offer the ability to invest in our securities.

#### Disclosure of Commission Position on Indemnification for Securities Act Liabilities

Our amended and restated bylaws provide for the indemnification of officers, directors and third parties acting on our behalf if such persons act in good faith and in a manner reasonably believed to be in and not opposed to our best interest, and, with respect to any criminal action or proceeding, such indemnified party had no reason to believe his or her conduct was unlawful.

To the extent that indemnification for liabilities arising under the Securities Act may be permitted to directors, officers or persons controlling our company pursuant to the foregoing provisions, we have been informed that, in the opinion of the SEC, this indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable. If a claim for indemnification against these liabilities (other than the payment by us of expenses incurred or paid by a director, officer or controlling person of our company in the successful defense of any action, suit or proceeding) is asserted by any of our directors, officers or controlling persons in connection with the securities being registered, we will, unless in the opinion of our counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether this indemnification by us is against public policy as expressed in the Securities Act and will be governed by the final adjudication of that issue.

#### Director Compensation

The following table sets forth a summary of the compensation we paid to our non-employee directors during 2013. Other than as set forth in the table below, we did not pay any compensation, make any equity awards or non-equity awards to, or pay any other compensation to any of the other non-employee members of our board of directors in 2013. Mr. Noyes received no compensation for his service as a director, and, consequently, is not included in this table.

Prior to this offering, we did not have a formal policy for compensating our non-employee directors. However, non-employee directors who are not affiliated with any of our major stockholders may receive stock options and other equity awards under our stock incentive plans from time to time as determined by our board of directors. We also reimburse non-employee directors for travel expenses incurred in connection with their duties as directors. We expect to adopt a new compensation program for our non-employee directors concurrent with the consummation of this offering. We are still considering the design of this program and have retained an independent compensation consultant to help us determine its terms.

<u>Name</u>	<u>Fees Earned or Paid in Cash</u>	<u>Stock Options</u>	<u>All Other Compensation</u>
Hubert Birner, Ph.D.	—	—	—
Todd Foley	—	—	—
F. Nicholas Franano, M.D.(1)	—	—	\$ 43,000
John G. Freund, M.D.	—	—	—
Brendan M. O'Leary, Ph.D.	—	—	—
Gregory D. Phelps(2)	\$ 20,000	—	—

(1) Amount represents consulting fees for services rendered by Dr. Franano.

(2) Amount represents annual director fee for Mr. Phelps. Amount was paid in equal quarterly installments.

**CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS**

Other than compensation arrangements, we describe below transactions and series of similar transactions, since January 1, 2011, to which we were a party or will be a party, in which:

- the amounts involved exceeded or will exceed \$120,000; and
- any of the directors, executive officers or holders of more than 5% of the capital stock of Proteon, or any member of the immediate family of the foregoing persons, had or will have a direct or indirect material interest.

Compensation arrangements for our directors and named executive officers are described elsewhere in this prospectus.

**Debt Financing**

In April 2013, we entered into a convertible note purchase agreement with beneficial owners of more than 5% of our capital stock, pursuant to which, in September 2013, we issued secured convertible promissory notes. The notes carried interest at 8% per annum. In May 2014, these notes were converted and the aggregate amount of outstanding principal and unpaid accrued interest thereon was exchanged for shares of our Series D convertible preferred stock, as described below under "—Series D Preferred Stock Financing." The following table sets forth the aggregate principal amount of promissory notes that we issued to our directors, executive officers and 5% stockholders, and their affiliates or immediate family members:

<u>Investor</u>	<u>Aggregate Principal Amount of Notes</u>
Intersouth Partners VI, L.P.	\$ 653,950
Prism Venture Partners and related funds	\$ 937,000
Skyline Venture Partners Qualified Purchaser Fund IV, LP	\$ 921,241
TVM Capital and related funds	\$ 1,172,529

**Preferred Stock Financing*****Series C Preferred Stock Financing***

In August 2011, we issued and sold to investors an aggregate of 13,202,932 shares of our Series C convertible preferred stock and warrants to purchase 10,471,282 shares of our common stock, at a purchase price of \$1.15 per share, for aggregate consideration of approximately \$15,183,371, which was paid for in cash. As of March 31, 2014, there are 10,471,282 shares of our common stock issuable upon exercise of outstanding warrants at a weighted average exercise price of \$0.29 per share. The following table sets forth the aggregate amount of securities that we issued to our directors, executive officers and 5% stockholders, and their affiliates or immediate family members in this transaction:

<u>Investor</u>	<u>Shares of Series C Preferred Stock Issued</u>	<u>Shares of Common Stock Underlying the Warrants</u>	<u>Purchase Price</u>
TVM Capital and related funds	3,130,434	2,482,757	\$ 3,599,999
Skyline Venture Partners Qualified Purchaser Fund IV, L.P.	2,436,437	1,932,346	\$ 2,801,903
Prism Venture Partners and related funds	2,478,183	1,965,454	\$ 2,849,910
Intersouth Partners VI, L.P.	1,729,523	1,371,690	\$ 1,988,951
MPM Bio IV NVS Strategic Fund, LP	1,645,073	1,304,713	\$ 1,891,834

**Series D Preferred Stock Financing**

On May 13, 2014, we issued and sold to investors an aggregate of 52,813,827 shares of our Series D convertible preferred stock, at a purchase price of \$0.588656 per share, for aggregate consideration of \$25,000,000. This included 10,344,201 shares of our Series D preferred stock that was paid for by converting of approximately \$4.5 million of principal indebtedness and unpaid accrued interest thereon under the promissory notes described above under "—Debt Financing", at a conversion price of \$0.4414 per share, which represented a 25% discount on the purchase price per share of our Series D convertible preferred stock issued and sold in the offering.

The following table sets forth the aggregate amount of securities that we issued to our directors, executive officers and 5% stockholders, and their affiliates or immediate family members in this transaction:

<u>Investor</u>	<u>Shares of Series D Preferred Stock Issued</u>	<u>Purchase Price</u>
Abingworth Bioventures VI, LP	16,044,081	\$ 9,444,445
Pharmstandard International S.A.	8,493,925	\$ 5,000,000
Deerfield and related funds	8,493,925	\$ 5,000,000
TVM Capital and related funds	5,005,486	\$ 2,534,850
Skyline Venture Partners Qualified Purchaser Fund IV, L.P.	3,932,747	\$ 1,991,600
Prism Venture Partners and related funds	4,000,070	\$ 2,025,698
Intersouth Partners VI, L.P.	2,319,806	\$ 1,135,974
MPM Bio IV NVS Strategic Fund, LP	1,765,137	\$ 1,039,058

**Investors' Rights Agreement**

In connection with our Series D convertible preferred stock financing, on May 13, 2014, we entered into the Fourth Amended and Restated Investors' Rights Agreement with the holders of all of our then-outstanding shares of preferred stock including certain of our executive officers and entities with which certain of our directors are affiliated. The agreement provides that these holders have the right to demand that we file a registration statement with respect to the common stock issued upon conversion of our preferred stock. These holders may also request that shares of common stock held by them be included in certain registration statements that we are otherwise filing. See "Description of Capital Stock—Registration Rights."

**Right of First Refusal and Co-Sale Agreement**

In connection with our Series D convertible preferred stock financing, on May 13, 2014, we entered into the Fourth Amended and Restated Right of First Refusal and Co-Sale Agreement with the holders of all of our then-outstanding shares of preferred stock including certain of our executive officers and entities with which certain of our directors are affiliated. Pursuant to the terms of this agreement, in the event of a proposed sale of shares of our common or preferred stock, the seller is required to first offer such shares to the company and to the other investors, subject to certain conditions and restrictions. This agreement will terminate upon the completion of this offering.

**Voting Agreement**

In connection with our Series D convertible preferred stock financing on May 13, 2014, we entered into the Fourth Amended and Restated Voting Agreement with the holders of all of our then outstanding shares of preferred stock including certain of our executive officers and entities with which certain of our directors are affiliated, with respect to the election of directors and certain other matters. All of our

current directors were elected pursuant to the terms of this agreement. This agreement will terminate upon the completion of this offering.

#### **Related Party Transactions Policy**

Prior to completion of the offering, we will adopt a related person transaction approval policy that will govern the review of related person transactions following the closing of this offering. Pursuant to this policy, if we want to enter into a transaction with a related person or an affiliate of a related person, our Chief Financial Officer will review the proposed transaction to determine, based on applicable NASDAQ and SEC rules, if such transaction requires pre-approval by the audit committee and/or board of directors. If pre-approval is required, the matters will be reviewed at the next regular or special audit committee and/or board of directors meeting. We may not enter into a related person transaction unless our Chief Financial Officer has either specifically confirmed in writing that no further reviews are necessary or that all requisite corporate reviews have been obtained.

#### **Indemnification of Directors and Officers**

Prior to the completion of this offering, we expect to enter into indemnification agreements with each of our directors and executive officers. These agreements will require us to indemnify these individuals and, in certain cases, affiliates of such individuals, to the fullest extent permissible under Delaware law against liabilities that may arise by reason of their service to us or at our direction, and to advance expenses incurred as a result of any proceeding against them as to which they could be indemnified.



**PRINCIPAL STOCKHOLDERS**

The following table sets forth information relating to the beneficial ownership of our common stock as of June 24, 2014, by: each person, or group of affiliated persons, known by us to beneficially own more than 5% of our outstanding shares of common stock; each of our directors; each of our named executive officers; and all of our directors and executive officers as a group.

The number of shares beneficially owned by each entity, person, director or executive officer is determined in accordance with the rules of the SEC, and the information is not necessarily indicative of beneficial ownership for any other purpose. Under such rules, beneficial ownership includes any shares over which the individual has sole or shared voting power or investment power as well as any shares that the individual has the right to acquire within 60 days of June 24, 2014 through the exercise of any stock option, warrants or other rights. Except as otherwise indicated, and subject to applicable community property laws, the persons named in the table have sole voting and investment power with respect to all shares of common stock held by that person.

The percentage of shares beneficially owned is computed on the basis of 138,752,338 shares of our common stock outstanding as of June 24, 2014, assuming for purposes of this table that all outstanding shares of our preferred stock have been converted to common stock and that the Series D convertible preferred stock converted on a one-for-one basis. For a description of the conversion, upon the completion of this offering, of shares of our Series D convertible preferred stock into shares of our common stock, see "Capitalization—Series D Convertible Preferred Stock." Shares of our common stock that a person has the right to acquire within 60 days of June 24, 2014 are deemed outstanding for purposes of computing the percentage ownership of the person holding such rights, but are not deemed outstanding for purposes of computing the percentage ownership of any other person, except with respect to the percentage ownership of all directors and executive officers as a group. Unless otherwise indicated below, the address for each beneficial owner listed is c/o Proteon Therapeutics, Inc., 200 West Street, Waltham, MA 02451.

<u>Beneficial Owner</u>	<u>Prior to the Offering</u>		<u>After the Offering</u>	
	<u>Number</u>	<u>Percent</u>	<u>Number</u>	<u>Percent</u>
<b>5% Stockholders:</b>				
TVM Capital and related funds(1)	25,950,984	18.4%		
Prism Venture Partners and related funds(2)	20,710,808	14.7		
Skyline Venture Partners Qualified Purchaser Fund IV, L.P.(3)	20,358,205	14.5		
Abingworth Bioventures VI, L.P.(4)	16,044,081	11.6		
Intersouth Partners VI, L.P.(5)	13,992,824	10.0		
MPM Bio IV NVS Strategic Fund, L.P.(6)	13,126,423	9.4		
Deerfield and related funds(7)	8,493,925	6.1		
Pharmstandard International S.A.(8)	8,493,925	6.1		
<b>Directors and Named Executive Officers:</b>				
Timothy P. Noyes(9)	6,125,355	4.2		
Gregory D. Phelps(10)	502,635	*		
Hubert Birner, Ph.D.(1)	25,950,984	18.4		
Brendan M. O'Leary, Ph.D.(2)	20,710,808	14.7		
John G. Freund, M.D.(3)	20,358,205	14.5		
Timothy Haines(4)	16,044,081	11.6		
F. Nicholas Franano, M.D.(11)	4,923,744	3.5		
Todd Foley(6)	13,126,423	9.4		
Dmitry Kobzyev(8)	8,493,925	6.1		
Steven K. Burke(12)	3,133,491	2.2		
Daniel P. Gottlieb(13)	983,816	*		
<b>All executive officers and directors as a group (12 persons)(14)</b>	<b>122,353,467</b>	<b>76.2%</b>		

\* Indicates ownership of less than one percent.

- (1) Includes (a) 17,477,906 shares of common stock issuable upon conversion of convertible preferred stock and warrants to purchase 1,849,034 shares of common stock held by TVM Life Science Ventures VI GmbH & Co. KG and (b) 5,990,321 shares of common stock issuable upon conversion of convertible preferred stock and warrants to purchase 633,723 shares of common stock held by TVM Life Science Ventures VI L.P. Excludes 1,316,683 shares of common stock issuable upon conversion of convertible preferred stock and 451,276 shares of common stock issuable upon conversion of convertible preferred stock that TVM Life Science Ventures VI GmbH & Co. KG and TVM Life Science Ventures VI L.P., respectively, have the right to acquire, which right cannot be exercised during the period commencing on the date that the Company submits a registration statement on Form S-1 to the SEC and ending on the earlier of (x) the third business day following the withdrawal of such registration statement on Form S-1 in connection with any abandonment of the IPO and (y) the closing of the IPO. Alexandra Goll, Helmut Schühlsler, Stefan Fischer, Axel Polack and Hubert Birner, our director, are members of the investment committee of TVM Life Science Ventures VI Management Limited Partnership, a special limited partner of TVM Life Science Ventures VI GMBH & Co. KG and TVM Life Science Ventures VI LP with voting and dispositive power over the share held by those entities. TVM Life Science Venture VI Management Limited Partnership and these individuals each disclaim beneficial ownership of such shares except to the extent of any pecuniary interest therein. The address for each of the individuals and entities listed above is c/o TVM Capital GmbH, Ottostrasse 4, 80333, Munich, Germany. Dr. Birner's address is c/o TVM Capital GmbH, Ottostrasse 4, 80333, Munich, Germany.
- (2) Includes (a) 12,879,940 shares of common stock issuable upon conversion of convertible preferred stock and warrants to purchase 1,350,465 shares of common stock held by Prism Venture Partners V, L.P., and (b) 5,865,414 shares of common stock and warrants to purchase 614,989 shares of common stock held by Prism Venture Partners V-A, L.P. Excludes 970,780 shares of common stock issuable upon conversion of convertible preferred stock and 442,085 shares of common stock issuable upon conversion of convertible preferred stock that Prism Venture Partners V, L.P. and Prism Venture Partners V-A, L.P., respectively, have the right to acquire, which right cannot be exercised during the period commencing on the date that the Company submits a registration statement on Form S-1 to the SEC and ending in the earlier of (x) the third business day following the withdrawal of such registration statement on Form S-1 in connection with any abandonment of the IPO and (y) the closing of the IPO. Steven J. Benson, James A. Counihan, and Brendan M. O'Leary are the managing members of Prism Venture Partners V, LLC, the sole general partner of Prism Investment Partners V, L.P., which is the sole general partner of Prism Venture Partners V, L.P. and Prism Venture Partners V-A, L.P. Each of the managing members disclaims beneficial ownership of any such shares except to the extent of his proportionate pecuniary interest therein. The address for Dr. O'Leary and Prism Venture Partners is c/o Prism VentureWorks, 75 Second Avenue, Suite 210, Needham, MA 02494.
- (3) Includes 18,425,859 shares of common stock issuable upon conversion of convertible preferred stock and warrants to purchase 1,932,346 shares of common stock. Excludes 1,389,064 shares of common stock issuable upon conversion of convertible preferred stock that the holder has the right to acquire, which right cannot be exercised during the period commencing on the date that the Company submits a registration statement on Form S-1 to the SEC and ending in the earlier of (a) the third business day following the withdrawal of such registration statement on Form S-1 in connection with any abandonment of the IPO and (b) the closing of the IPO. Skyline Venture Management IV, LLC ("SVM VI") is the sole general partner of Skyline Venture Partners Qualified Purchaser Fund IV, L.P. ("SVPQP IV"). Each of John G. Freund, our director, Yasunori Kaneko and Stephen Hoffman are managing directors of SVM IV and share voting and dispositive power over the shares held by the SVPQP IV; however, they disclaim beneficial ownership of the shares held by SVPQP IV, except to the extent of their pecuniary interests therein. The address for Dr. Freund and Skyline Venture Partners Qualified Purchaser Fund IV, L.P. is 525 University Avenue, Suite 520, Palo Alto, CA 94301.
- (4) Includes 16,044,081 shares of common stock issuable upon conversion of convertible preferred stock. Excludes 12,835,264 shares of common stock issuable upon conversion of convertible preferred stock that the holder has the right to acquire, which right cannot be exercised during the period commencing on the date that the Company submits a registration statement on Form S-1 to the SEC

and ending in the earlier of (a) the third business day following the withdrawal of such registration statement on Form S-1 in connection with any abandonment of the IPO and (b) the closing of the IPO. Abingworth Bioventures VI GP LP, a Scottish limited partnership, serves as the general partner of Abingworth Bioventures VI LP ("ABV VI"). Abingworth General Partner VI LLP, an English limited liability partnership, serves as the general partner of Abingworth Bioventures VI GP LP. ABV VI (acting by its general partner Abingworth Bioventures VI GP LP, acting by its general partner Abingworth General Partner VI LLP) has delegated to Abingworth LLP, an English limited liability partnership, all investment and dispositive power over the securities held by ABV VI. An investment committee of Abingworth LLP, comprised of Joseph Anderson, Michael F. Bigham, Stephen W. Bunting, Genghis Lloyd-Harris, and Timothy Haines, our director, approves investment and voting decisions by a majority vote, and no individual member has the sole control or voting power over the securities held by ABV VI. Each of Abingworth Bioventures VI GP LP, Abingworth General Partner VI LLP, Joseph Anderson, Michael F. Bigham, Stephen W. Bunting, Genghis Lloyd-Harris, and Timothy Haines disclaims beneficial ownership of the securities held by the ABV VI except to the extent of their proportionate pecuniary interest therein. The address of the principal place of business of each of the entities and individuals listed above is c/o Abingworth LLP, Princes House, 38 Jermyn Street, London, England SW1Y 6DN.

- (5) Includes 12,621,134 shares of common stock issuable upon conversion of convertible preferred stock and warrants to purchase 1,371,690 shares of common stock. Excludes 608,529 shares of common stock issuable upon conversion of convertible preferred stock that the holder has the right to acquire, which right cannot be exercised during the period commencing on the date that the Company submits a registration statement on Form S-1 to the SEC and ending in the earlier of (a) the third business day following the withdrawal of such registration statement on Form S-1 in connection with any abandonment of the IPO and (b) the closing of the IPO. Dennis J. Dougherty and Mitchell Mumma are the managing partners of Intersouth Associates VI, LLC, the general partner of Intersouth Partners VI, L.P. Each of the managing partners disclaims beneficial ownership of any such shares except to the extent of his proportionate pecuniary interest therein. The address for Intersouth Partners VI, L.P. is 102 City Hall Plaza, Suite 200, Durham, NC 27701.
- (6) Includes 11,821,710 shares of common stock issuable upon conversion of convertible preferred stock and warrants to purchase 1,304,713 shares of common stock. Excludes 1,412,109 shares of common stock issuable upon conversion of convertible preferred stock that the holder has the right to acquire, which right cannot be exercised during the period commencing on the date that the Company submits a registration statement on Form S-1 to the SEC and ending in the earlier of (a) the third business day following the withdrawal of such registration statement on Form S-1 in connection with any abandonment of the IPO and (b) the closing of the IPO. Todd Foley, our director, is a Member of MPM BioVentures IV LLC, which is the General Partner of MPM BioVentures IV GP LLC, which is the General Partner of MPM Bio IV NVS Strategic Fund, L.P. Mr. Foley shares the power to vote, hold and dispose of the shares held by MPM Bio IV NVS Strategic Fund, L.P. Mr. Foley disclaims beneficial ownership of any such shares except to the extent of his proportionate pecuniary interest therein. The address for Mr. Foley and MPM Bio IV NVS Strategic Fund, L.P. is 200 Clarendon Street, 54th Floor, Boston, MA 02116.
- (7) Includes (a) 6,134,501 shares of common stock issuable upon conversion of convertible preferred stock held by Deerfield Private Design Fund III, L.P., (b) 1,311,840 shares of common stock issuable upon conversion of convertible preferred stock held by Deerfield Special Situations Fund, L.P., and (c) 1,047,584 shares of common stock issuable upon conversion of convertible preferred stock held by Deerfield Special Situations International Master Fund, L.P. Excludes 4,907,601 shares of common stock issuable upon conversion of convertible preferred stock, 1,049,472 shares of common stock issuable upon conversion of convertible preferred stock and 838,067 shares of common stock issuable upon conversion of convertible preferred stock that Deerfield Private Design Fund III, L.P., Deerfield Special Situations Fund, L.P. and Deerfield Special Situations International Master Fund, L.P., respectively, have the right to acquire, which right cannot be exercised during the period commencing on the date that the Company submits a registration statement on Form S-1 to the SEC and ending in the earlier of (x) the third business day following the withdrawal of such registration statement on Form S-1 in connection with any abandonment of the IPO and (y) the closing of the IPO. Deerfield

Mgmt, L.P. is the general partner of each of Deerfield Special Situations Fund, L.P. and Deerfield Special Situations International Master Fund, L.P. Deerfield Mgmt III, L.P. is the general partner of Deerfield Private Design Fund III, L.P. (together with Deerfield Special Situations Fund, L.P. and Deerfield Special Situations International Master Fund, L.P., the "Deerfield Funds"). Deerfield Management Company, L.P. is the investment manager of each of the Deerfield Funds. Mr. James E. Flynn is the sole member of the general partner of each of Deerfield Mgmt, L.P., Deerfield Mgmt III, L.P. and Deerfield Management Company, L.P. Deerfield Mgmt, L.P. may be deemed to beneficially own the shares held by Deerfield Special Situations Fund, L.P. and Deerfield Special Situations International Master Fund, L.P., Deerfield Mgmt III, L.P. may be deemed to beneficially own the shares held by Deerfield Private Design Fund III, L.P. Each of Deerfield Management Company, L.P. and Mr. Flynn may be deemed to beneficially own the shares held by the Deerfield Funds. The address of Deerfield Funds is 780 Third Avenue, 37<sup>th</sup> Floor, New York, NY 10017.

- (8) Includes 8,493,925 shares of common stock issuable upon conversion of convertible preferred stock. Excludes 6,795,140 shares of common stock issuable upon conversion of convertible preferred stock that the holder has the right to acquire, which right cannot be exercised during the period commencing on the date that the Company submits a registration statement on Form S-1 to the SEC and ending in the earlier of (a) the third business day following the withdrawal of such registration statement on Form S-1 in connection with any abandonment of the IPO and (b) the closing of the IPO. Pharmstandard International S.A. is a wholly owned subsidiary of public joint stock company "Pharmstandard." As the parent entity Pharmstandard has voting and investment control over the shares of the Company held by Pharmstandard International S.A. Dmitry Kobzyev, our director, is the representative of Pharmstandard International S.A. Dr. Kobzyev disclaims beneficial ownership of any such shares except to the extent of his proportionate pecuniary interest therein. The address for Dr. Kobzyev and Pharmstandard International S.A. is 65, Boulevard Grande Duchesse Charlotte, L-1331 Luxembourg, Grand-Duchy of Luxembourg.
- (9) Includes 6,125,355 shares of common stock which Mr. Noyes has the right to acquire upon the exercise of stock options that were exercisable as of June 24, 2014, or that will become exercisable within 60 days after that date.
- (10) Includes 502,635 shares of common stock which Mr. Phelps has the right to acquire upon the exercise of stock options that were exercisable as of June 24, 2014, or that will become exercisable within 60 days after that date.
- (11) Includes (a) 3,457,453 shares of common stock and 88,666 shares of common stock issuable upon conversion of convertible preferred stock held directly by Dr. Franano, (b) 6,567 shares of common stock issuable upon conversion of convertible preferred stock held by Mr. Franano and Lorie Beth Whitaker, and (c) 1,352,757 shares of common stock which Dr. Franano has the right to acquire upon the exercise of stock options that were exercisable as of June 24, 2014, or that will become exercisable within 60 days after that date.
- (12) Includes 3,133,491 shares of common stock which Dr. Burke has the right to acquire upon the exercise of stock options that were exercisable as of June 24, 2014, or that will become exercisable within 60 days after that date.
- (13) Includes 983,816 shares of common stock which Mr. Gottlieb has the right to acquire upon the exercise of stock options that were exercisable as of June 24, 2014, or that will become exercisable within 60 days after that date.
- (14) Includes 14,098,054 shares of common stock which the directors and executive officers have the right to acquire upon the exercise of stock options that were exercisable as of June 24, 2014, or that will become exercisable within 60 days after that date.

## DESCRIPTION OF CAPITAL STOCK

The following description of our capital stock and provisions of our amended and restated certificate of incorporation, amended and restated bylaws and investors' rights agreement are summaries and are qualified by reference to the amended and restated certificate of incorporation and amended and restated bylaws that will become effective upon the closing of this offering as well as to those provisions of the investors rights' agreement that will remain in effect following the closing. We have filed copies of these documents with the SEC as exhibits to our registration statement of which this prospectus forms a part. The description of our capital stock reflects changes to our capital structure that will occur upon the closing of this offering. Currently, there is no established public trading market for our common stock.

### General

As of June 24, 2014, we had issued and outstanding:

- 3,814,856 shares of our common stock;
- 120,318,776 shares of our convertible preferred stock that will automatically convert into 134,918,694 shares of our common stock upon the closing of this offering;
- warrants to purchase a total of 10,471,282 shares of our common stock with a weighted-average exercise price of \$0.29 per share that we expect to be exercised immediately prior to the closing of this offering; and
- options to purchase a total of 17,982,120 shares of our common stock with a weighted-average exercise price of \$0.22 per share.

### Common Stock

**Voting Rights.** Each holder of our common stock is entitled to one vote for each share on all matters submitted to a vote of the stockholders, including the election of directors. Our stockholders do not have cumulative voting rights in the election of directors. Accordingly, the holders of a majority of the voting shares are able to elect all of the directors.

**Dividends.** Subject to preferences that may be applicable to any then outstanding preferred stock, holders of our common stock are entitled to receive dividends, if any, as may be declared from time to time by our board of directors out of legally available funds.

**Liquidation.** In the event of our liquidation, dissolution or winding up, holders of our common stock will be entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of all of our debts and other liabilities and the satisfaction of any liquidation preference granted to the holders of any then outstanding shares of preferred stock.

**Rights and Preferences.** Holders of common stock have no preemptive, conversion or subscription rights and there are no redemption or sinking fund provisions applicable to the common stock. The rights, preferences and privileges of the holders of common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of preferred stock that we may designate in the future.

### Preferred Stock

Immediately prior to this offering, our certificate of incorporation provided for five series of preferred stock. As of June 24, 2014, we had outstanding an aggregate of 120,318,776 shares of preferred stock held of record by 60 stockholders.

Upon closing of this offering, all outstanding shares of preferred stock will be automatically converted into \_\_\_\_\_ shares of our common stock. Under our amended and restated certificate of incorporation, our board of directors will have the authority, without further action by the stockholders, to

issue up to \_\_\_\_\_ shares of preferred stock in one or more series, to establish from time to time the number of shares to be included in each such series, to fix the rights, preferences and privileges of the shares of each wholly unissued series and any qualifications, limitations or restrictions thereon and to increase or decrease the number of shares of any such series, but not below the number of shares of such series then outstanding.

Our board of directors may authorize the issuance of preferred stock with voting or conversion rights that could adversely affect the voting power or other rights of the holders of the common stock. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions and other corporate purposes, could, among other things, have the effect of delaying, deferring or preventing a change in our control that may otherwise benefit holders of our common stock and may adversely affect the market price of the common stock and the voting and other rights of the holders of common stock. We have no current plans to issue any shares of preferred stock.

#### **Warrants**

As of June 24, 2014, we had outstanding warrants to purchase an aggregate of 10,471,282 shares of common stock at a weighted average exercise price of \$0.29, which we expect to be exercised in full immediately prior to the closing of the offering.

#### **Registration Rights**

After our initial public offering, certain holders of shares of our common stock, including those shares of our common stock that will be issued upon conversion of our preferred stock in connection with this offering, and those shares of our common stock that are issuable pursuant to our outstanding preferred stock warrants, or warrant shares, will be entitled to certain rights with respect to registration of such shares under the Securities Act. These shares are collectively referred to herein as registrable shares.

Under our Fourth Amended and Restated Investors' Rights Agreement, holders of registrable shares (other than warrant shares) can demand that we file a registration statement or request that their shares be included on a registration statement that we are otherwise filing, in either case, registering the resale of their shares of common stock. These registration rights are subject to conditions and limitations, including the right, in certain circumstances, of the underwriters of an offering to limit the number of shares included in such registration and our right, in certain circumstances, not to effect a requested registration on Form S-1 or Form S-3 within 90 days before or 180 days following our estimated date of filing of a registration statement pertaining to an underwritten public offering of securities for our account, including this offering.

These registration rights are contained in our investors' rights agreement, which is described under "Certain Relationships and Related Transactions—Investors' Rights Agreement" above and a copy of which will be filed as an exhibit to the registration statement of which this prospectus is a part.

#### **Anti-Takeover Effects of Provisions of Delaware Law and Our Amended and Restated Certificate of Incorporation and Amended and Restated Bylaws**

Our amended and restated certificate of incorporation and amended and restated bylaws will contain certain provisions that are intended to enhance the likelihood of continuity and stability in the composition of the board of directors and which may have the effect of delaying, deferring or preventing a future takeover or change in control of the company unless such takeover or change in control is approved by the board of directors. These provisions include:

**Classified Board.** Our amended and restated certificate of incorporation will provide that our board of directors will be divided into three classes of directors, with the classes as nearly equal in number as possible. As a result, approximately one-third of our board of directors will be elected each year. The

classification of directors will have the effect of making it more difficult for stockholders to change the composition of our board. Our amended and restated certificate of incorporation will also provide that, subject to any rights of holders of preferred stock to elect additional directors under specified circumstances, the number of directors will be fixed exclusively pursuant to a resolution adopted by our board of directors. Upon completion of this offering, we expect that our board of directors will have nine members.

**Action by Written Consent; Special Meetings of Stockholders.** Our certificate of incorporation will provide that stockholder action can be taken only at an annual or special meeting of stockholders and cannot be taken by written consent in lieu of a meeting. Our amended and restated certificate of incorporation and our amended and restated bylaws will also provide that, except as otherwise required by law, special meetings of the stockholders can be called only by or at the direction of the board of directors pursuant to a resolution adopted by a majority of the total number of directors. Except as described above, stockholders will not be permitted to call a special meeting or to require the board of directors to call a special meeting.

**Removal of Directors.** Our certificate of incorporation will provide that our directors may be removed only for cause by the affirmative vote of at least 75% of the voting power of our outstanding shares of capital stock, voting together as a single class. This requirement of a supermajority vote to remove directors could enable a minority of our stockholders to prevent a change in the composition of our board.

**Advance Notice Procedures.** Our amended and restated bylaws will establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to the board of directors. Stockholders at an annual meeting will only be able to consider proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of the board of directors or by a stockholder who was a stockholder of record on the record date for the meeting, who is entitled to vote at the meeting and who has given our Secretary timely written notice, in proper form, of the stockholder's intention to bring that business before the meeting. Although the amended and restated bylaws will not give the board of directors the power to approve or disapprove stockholder nominations of candidates or proposals regarding other business to be conducted at a special or annual meeting, the amended and restated bylaws may have the effect of precluding the conduct of certain business at a meeting if the proper procedures are not followed or may discourage or deter a potential acquirer from conducting a solicitation of proxies to elect its own slate of directors or otherwise attempting to obtain control of the company.

**Super Majority Approval Requirements.** The Delaware General Corporation Law generally provides that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation's certificate of incorporation or amended and restated bylaws, unless either a corporation's certificate of incorporation or bylaws requires a greater percentage. Our amended and restated certificate of incorporation and amended and restated bylaws will provide that the affirmative vote of holders of at least 75% of the total votes eligible to be cast in the election of directors will be required to amend, alter, change or repeal the amended and restated bylaws. This requirement of a supermajority vote to approve amendments to our amended and restated bylaws could enable a minority of our stockholders to exercise veto power over any such amendments.

**Authorized but Unissued Shares.** Our authorized but unissued shares of common stock and preferred stock will be available for future issuance without stockholder approval. These additional shares may be utilized for a variety of corporate purposes, including future public offerings to raise additional capital, corporate acquisitions and employee benefit plans. The existence of authorized but unissued shares of common stock and preferred stock could render more difficult or discourage an attempt to obtain control of a majority of our common stock by means of a proxy contest, tender offer, merger or otherwise.

**Exclusive Forum.** Our amended and restated certificate of incorporation will provide that, subject to limited exceptions, the state or federal courts located in the State of Delaware will be the sole and

exclusive forum for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or other employees to us or our stockholders, (iii) any action asserting a claim against us arising pursuant to any provision of the Delaware General Corporation Law, our amended and restated certificate of incorporation or our amended and restated bylaws, or (iv) any other action asserting a claim against us that is governed by the internal affairs doctrine. Any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock shall be deemed to have notice of and to have consented to the provisions of our amended and restated certificate of incorporation described above. Although we believe these provisions benefit us by providing increased consistency in the application of Delaware law for the specified types of actions and proceedings, the provisions may have the effect of discouraging lawsuits against our directors and officers. The enforceability of similar choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that, in connection with one or more actions or proceedings described above, a court could find the choice of forum provisions contained in our certificate of incorporation to be inapplicable or unenforceable.

### ***Section 203 of the Delaware General Corporation Law***

Upon completion of this offering, we will be subject to the provisions of Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a publicly-held Delaware corporation from engaging in a "business combination" with an "interested stockholder" for a three-year period following the time that this stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. A "business combination" includes, among other things, a merger, asset or stock sale or other transaction resulting in a financial benefit to the interested stockholder. An "interested stockholder" is a person who, together with affiliates and associates, owns, or did own within three years prior to the determination of interested stockholder status, 15% or more of the corporation's voting stock. Under Section 203, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions: before the stockholder became interested, the board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder; upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, shares owned by persons who are directors and also officers, and employee stock plans, in some instances; or at or after the time the stockholder became interested, the business combination was approved by the board of directors of the corporation and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder. A Delaware corporation may "opt out" of these provisions with an express provision in its original certificate of incorporation or an express provision in its certificate of incorporation or bylaws resulting from a stockholders' amendment approved by at least a majority of the outstanding voting shares. We have not opted out of these provisions. As a result, mergers or other takeover or change in control attempts of us may be discouraged or prevented.

### ***Transfer Agent and Registrar***

The transfer agent and registrar for our common stock is .

### ***Listing***

We expect to apply for listing of our common stock on the NASDAQ Global Market under the symbol "PRTO."



## SHARES ELIGIBLE FOR FUTURE SALE

Prior to this offering, there has been no public market for our common stock. Future sales of our common stock, including shares issued upon the exercise of outstanding options or warrants, in the public market after this offering, or the perception that those sales may occur, could cause the prevailing market price for our common stock to fall or impair our ability to raise equity capital in the future. As described below, only a limited number of shares of our common stock will be available for sale in the public market for a period of several months after completion of this offering due to contractual and legal restrictions on resale described below. Future sales of our common stock in the public market either before (to the extent permitted) or after restrictions lapse, or the perception that those sales may occur, could adversely affect the prevailing market price of our common stock at such time and our ability to raise equity capital at a time and price we deem appropriate.

### Sale of Restricted Shares

As of June 24, 2014, based on the number of shares of our common stock then outstanding, upon the closing of this offering and assuming (1) the conversion of our outstanding preferred stock into common stock, (2) no exercise of the underwriters' option to purchase additional shares of common stock, and (3) no exercise of outstanding options or warrants, we would have had outstanding an aggregate of approximately 75,260,798 shares of common stock. Of these shares, all of the \_\_\_\_\_ shares of common stock to be sold in this offering, and any shares sold upon exercise of the underwriters' option to purchase additional shares will be freely tradable in the public market without restriction or further registration under the Securities Act, unless the shares are held by any of our "affiliates" as such term is defined in Rule 144 of the Securities Act. All remaining shares of common stock held by existing stockholders immediately prior to the completion of this offering will be "restricted securities" as such term is defined in Rule 144. These restricted securities were issued and sold by us, or will be issued and sold by us, in private transactions and are eligible for public sale only if registered under the Securities Act or if they qualify for an exemption from registration under the Securities Act, including the exemptions provided by Rule 144 or Rule 701, which rules are summarized below.

As a result of the lock-up agreements referred to below and the provisions of Rule 144 and Rule 701 under the Securities Act, the shares of our common stock (excluding the shares sold in this offering) that will be available for sale in the public market are as follows:

#### Approximate Number of Shares

#### First Date Available for Sale into Public Market

180 days after the date of this prospectus upon expiration of the lock up agreements referred to below, subject in some cases to applicable volume limitations under Rule 144.

#### *Lock-up Agreements*

In connection with this offering, we, our directors, our officers and stockholders beneficially owning approximately \_\_\_\_\_ % of our shares of common stock outstanding as of March 31, 2014 (assuming conversion of all of our outstanding shares of preferred stock and warrants), have agreed with the underwriters not to dispose of or hedge any shares of our common stock or securities convertible into or exchangeable for shares of common stock during the period from the date of the lock-up agreement continuing through the date 180 days after the date of this prospectus, except with the prior written consent of \_\_\_\_\_ and \_\_\_\_\_, the representatives of the underwriters. The representatives of the underwriters have advised us that they have no current intent or arrangement to release any of the shares subject to the lock-up agreements prior to the expiration of the lock-up period.

The lock-up agreements do not contain any pre-established conditions to the waiver by Stifel, Nicolaus & Company, Incorporated and JMP Securities LLC on behalf of the underwriters of any terms of the lock-up agreements. Any determination to release shares subject to the lock-up agreements would be based on a number of factors at the time of determination, including but not necessarily limited to the market price of the common stock, the liquidity of the trading market for the common stock, general market conditions, the number of shares proposed to be sold, contractual obligations to release certain shares subject to the lock-up agreements in the event any such shares are released, subject to certain specific limitations and thresholds, and the timing, purpose and terms of the proposed sale.

Following the lock-up periods set forth in the agreements described above, and assuming that the representatives of the underwriters do not release any parties from these agreements, all of the shares of our common stock that are restricted securities or are held by our affiliates as of the date of this prospectus will be eligible for sale in the public market in compliance with Rule 144 under the Securities Act.

In addition to the restrictions contained in the lock-up agreements described above, we have entered into agreements with certain of our security holders, including our amended and restated investors rights agreement and our standard forms of option agreements under our equity incentive plan, that contain market stand-off provisions imposing restrictions on the ability of such security holders to offer, sell or transfer our equity securities for a period of 180 days following the date of this prospectus.

#### *Rule 144*

In general, persons who have beneficially owned restricted shares of our common stock for at least six months, and any affiliate of the Company who owns either restricted shares of our common stock, are entitled to sell their securities without registration with the SEC under an exemption from registration provided by Rule 144 under the Securities Act.

#### *Non-Affiliates*

Any person who is not deemed to have been one of our affiliates at the time of, or at any time during the three months preceding, a sale may sell an unlimited number of restricted securities under Rule 144 if:

- the restricted securities have been held for at least six months, including the holding period of any prior owner other than one of our affiliates;
- we have been subject to the Exchange Act periodic reporting requirements for at least 90 days before the sale; and
- we are current in our Exchange Act reporting at the time of sale.

Any person who is not deemed to have been an affiliate of ours at the time of, or at any time during the three months preceding, a sale and has held the restricted securities for at least one year, including the holding period of any prior owner other than one of our affiliates, will be entitled to sell an unlimited number of restricted securities without regard to the length of time we have been subject to Exchange Act periodic reporting or whether we are current in our Exchange Act reporting.

#### *Affiliates*

Persons seeking to sell restricted securities who are our affiliates at the time of, or any time during the three months preceding, a sale would be subject to the restrictions described above. They are also subject to additional restrictions, by which such person would be required to comply with the manner of sale and notice provisions of Rule 144 and would be entitled to sell within any three-month period only that number of securities that does not exceed the greater of either of the following:

- 1% of the number of shares of our common stock then outstanding, which will equal approximately \_\_\_\_\_ shares immediately after the completion of this offering based on the number of shares outstanding as of \_\_\_\_\_; or

- the average weekly trading volume of our common stock on the NASDAQ Global Market during the four calendar weeks preceding the filing of a notice on Form 144 with respect to the sale.

### **Rule 701**

In general, under Rule 701 a person who purchased shares of our common stock pursuant to a written compensatory plan or contract and who is not deemed to have been one of our affiliates during the immediately preceding 90 days may sell these shares in reliance upon Rule 144, but without being required to comply with the notice, manner of sale or public information requirements or volume limitation provisions of Rule 144. Rule 701 also permits affiliates to sell their Rule 701 shares under Rule 144 without complying with the holding period requirements of Rule 144. All holders of Rule 701 shares, however, are required to wait until 90 days after the date of this prospectus before selling such shares pursuant to Rule 701. Substantially all Rule 701 shares are subject to lock-up agreements as described below and in the section of this prospectus titled "Underwriting" and will become eligible for sale upon the expiration of the restrictions set forth in those agreements.

### **Registration Rights**

Upon the completion of this offering, the holders of \_\_\_\_\_ shares of our common stock issuable upon the conversion of our preferred stock, or their transferees, will be entitled to specified rights with respect to the registration of the offer and sale of their shares under the Securities Act. Registration of the offer and sale of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act immediately upon the effectiveness of the registration. See the section of this prospectus titled "Description of Capital Stock—Registration Rights" for additional information.

### **Equity Incentive Plans**

We intend to file with the SEC one or more registration statements on Form S-8 under the Securities Act covering the shares of common stock that we may issue upon exercise of outstanding options reserved for issuance under our 2006 Equity Incentive Plan and/or 2014 Equity Incentive Plan. This registration statement is expected to be filed and become effective as soon as practicable after the completion of this offering. Accordingly, shares registered under this registration statement will be available for sale in the open market following its effective date, subject to Rule 144 volume limitations and the lock-up agreements described above, if applicable.

## **MATERIAL UNITED STATES FEDERAL INCOME TAX CONSEQUENCES TO NON-U.S. HOLDERS OF OUR COMMON STOCK**

The following is a summary of the material U.S. federal income tax consequences of the acquisition, ownership, and disposition of our common stock by a non-U.S. holder that purchases shares of our common stock for cash in this offering. For purposes of this summary, a "non-U.S. holder" means a beneficial owner of our common stock that is, for U.S. federal income tax purposes:

- an individual who is not a citizen or resident of the United States;
- a corporation (or an entity treated as a corporation for U.S. federal income tax purposes) that is created or organized under the laws of a jurisdiction other than the United States, any state thereof, or the District of Columbia;
- a foreign estate (i.e., an estate other than an estate the income of which is subject to U.S. federal income taxation regardless of its source); or
- a foreign trust (i.e., a trust other than a trust (i) with respect to which a court within the United States is able to exercise primary supervision over its administration and one or more U.S. persons (as defined in Section 386 of the Internal Revenue Code of 1986, as amended, the Code) have the authority to control all substantial decisions or (ii) that has in effect a valid election under the applicable Treasury regulations to be treated as a United States person).

In the case of a holder that is classified as a partnership for U.S. federal income tax purposes, the tax treatment of a person treated as a partner in that partnership for U.S. federal income tax purposes generally will depend upon the status of the partner and the activities of the partner and the partnership. Partnerships and other entities treated as partnerships for U.S. federal income tax purposes and persons holding our common stock through a partnership or such entity should consult with their own tax advisors.

This summary is based upon the provisions of the Code, the U.S. Treasury regulations promulgated thereunder, judicial decisions, and published rulings and administrative procedures of the Internal Revenue Service, or the IRS, all as in effect as of the date hereof. These authorities are subject to differing interpretations and to change, possibly with retroactive effect, which could result in U.S. federal income tax consequences different from those summarized below. No ruling has been or will be sought from the IRS with respect to the matters summarized below, and there can be no assurance that the IRS will not take a contrary position regarding the U.S. federal income tax consequences of the acquisition, ownership, or disposition of our common stock, or that any such contrary position would not be sustained by a court.

This summary is not a complete analysis of all of the potential U.S. federal income tax consequences relating to the acquisition, ownership, and disposition of our common stock by non-U.S. holders, nor does it address any U.S. federal estate or gift tax consequences, any tax consequences arising under any state, local, or foreign tax laws, any consequences under the unearned income Medicare contribution tax enacted by the Health Care and Education Reconciliation Act of 2010, or any consequences under other U.S. federal tax laws (including the alternative minimum tax). In addition, this discussion does not address tax consequences resulting from a non-U.S. holder's particular circumstances or to non-U.S. holders that may be subject to special tax rules, including, without limitation:

- partnerships, other pass-through entities, or beneficial owners of interests in those entities;
- foreign governments or entities they control;
- "controlled foreign corporations" and their shareholders;
- "passive foreign investment companies" and their shareholders;
- corporations that accumulate earnings to avoid U.S. federal income tax;
- U.S. expatriates or former long-term residents of the United States;
- banks, insurance companies or other financial institutions;
- persons subject to the alternative minimum tax;
- tax-exempt pension funds or other tax-exempt organizations;
- tax-qualified retirement plans;

- traders, brokers, or dealers in securities, commodities, or currencies;
- persons that own or have owned, or are deemed to own or have owned, more than 5% of our common stock (except to the extent specifically set forth below);
- persons who hold our common stock as a position in a hedging transaction, "straddle," "conversion transaction" or other risk reduction transaction;
- persons who do not hold our common stock as a capital asset within the meaning of Section 1221 of the Code (generally, for investment purposes);
- persons deemed to sell our common stock under the constructive sale provisions of the Code; or
- persons who hold or receive our common stock pursuant to the exercise of any employee stock option or otherwise as compensation.

Prospective investors should consult their tax advisors regarding the particular U.S. federal income tax consequences to them of acquiring, owning, and disposing of our common stock, as well as any tax consequences arising under any state, local, or foreign tax laws and any other U.S. federal tax laws.

### **Distributions on Common Stock**

As described in the section entitled "Dividend Policy," we have never paid any dividends on our common stock and do not anticipate doing so in the foreseeable future. The disclosure in this section addresses the consequences should our board of directors, in the future, determine to make a distribution of cash or property with respect to our common stock (other than certain distributions of stock which may be made free of tax), or to effect a redemption that is treated for tax purposes as a distribution. Any such distribution will constitute a dividend for U.S. federal tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. To the extent such a distribution exceeds both our current and our accumulated earnings and profits, such excess will be allocated ratably among the shares of common stock with respect to which the distribution is made, will constitute a return of capital, and will first be applied against and reduce the non-U.S. holder's adjusted tax basis in those shares of common stock, but not below zero. Distributions in excess of our current and accumulated earnings and profits and in excess of a non-U.S. holder's tax basis in that non-U.S. holder's shares of common stock then will be treated as gain from the sale of that common stock, subject to the tax treatment described below under "Gain on Disposition of Common Stock." A non-U.S. holder's adjusted tax basis in a share of common stock is generally the purchase price of the share, reduced by the amount of any distributions constituting a return of capital with respect to that share.

Any dividend paid to a non-U.S. holder of our common stock generally will be subject to U.S. federal withholding tax at a rate of 30% of the gross amount of the dividend, or such lower rate as may be specified by an applicable income tax treaty. If a non-U.S. holder is eligible for benefits under an income tax treaty and wishes to claim a reduced rate of withholding, the non-U.S. holder generally will be required to provide us or our paying agent with a properly completed IRS Form W-8BEN, Form W-8BEN-E, or other applicable form, certifying under penalties of perjury the non-U.S. holder's qualification for the reduced rate. This certification must be provided to us or our paying agent prior to the payment of the dividend and may be required to be updated periodically. Special certification requirements apply to non-U.S. holders that hold common stock through certain foreign intermediaries. Non-U.S. holders that do not timely provide the required certifications, but that qualify for a reduced treaty rate, may obtain a refund of any excess amounts withheld by timely filing an appropriate claim for refund with the IRS. If we are not able to determine whether or not a distribution will exceed current and accumulated earnings and profits at the time the distribution is made, we may withhold tax on the entire amount of any distribution at the same rate as we would withhold on a dividend. However, a non-U.S. holder may obtain a refund of amounts that we withhold to the extent attributable to the portion of the distribution in excess of our current and accumulated earnings and profits.

If a non-U.S. holder holds our common stock in connection with the conduct of a trade or business in the United States, and dividends paid on the common stock are effectively connected with the non-U.S.

holder's U.S. trade or business (and, if required by an applicable income tax treaty, are attributable to a permanent establishment or fixed base maintained by the non-U.S. holder in the United States, as defined under the applicable treaty), the non-U.S. holder will be exempt from U.S. federal withholding tax on the dividends. To claim the exemption, the non-U.S. holder must furnish a properly executed IRS Form W-8ECI (or other applicable form) prior to the payment of the dividends. Any dividends paid on our common stock that are effectively connected with a non-U.S. holder's U.S. trade or business (and satisfy any other applicable treaty requirements) generally will be subject to U.S. federal income tax on a net income basis at the regular graduated U.S. federal income tax rates generally applicable to U.S. persons or at such lower rate as may be specified by an applicable income tax treaty. A non-U.S. holder that is treated as a corporation for U.S. federal income tax purposes also may be subject to an additional branch profits tax equal to 30% (or such lower rate as is specified by an applicable income tax treaty) of a portion of its earnings and profits for the taxable year that are effectively connected with a U.S. trade or business, as adjusted for certain items.

### **Gain on Disposition of Common Stock**

Subject to the discussions under "—Information Reporting and Backup Withholding" and "Foreign Account Tax Compliance Act," a non-U.S. holder generally will not be subject to U.S. federal income tax on any gain realized upon the sale, exchange, or other taxable disposition of our common stock unless:

- the gain is effectively connected with the non-U.S. holder's conduct of a U.S. trade or business (and, if required by an applicable income tax treaty, the gain is attributable to a permanent establishment or fixed base maintained by the non-U.S. holder in the United States), in which case the non-U.S. holder will be required to pay tax on the net gain derived from the sale, exchange, or other taxable disposition (net of certain deductions or credits) under regular graduated U.S. federal income tax rates generally applicable to U.S. persons or at such lower rate as may be specified by an applicable income tax treaty, and in the case of a non-U.S. holder that is treated as a corporation for U.S. federal income tax purposes, such non-U.S. holder may be subject to a branch profits tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty;
- the non-U.S. holder is an individual who is present in the United States for a period or periods aggregating 183 days or more during the taxable year in which the sale, exchange, or other taxable disposition occurs and certain other conditions are met, in which case the non-U.S. holder will be subject to U.S. federal income tax at a flat 30% rate (or such lower rate as is specified by an applicable income tax treaty) on the gain derived from the sale, exchange, or other taxable disposition, which gain may be offset by U.S. source capital losses (even though the non-U.S. holder is not considered a resident of the United States) provided that the non-U.S. holder has timely filed U.S. federal income tax returns reporting those losses; or
- our common stock is a U.S. real property interest by reason of our status as a U.S. real property holding corporation, or a USRPHC, for U.S. federal income tax purposes.

We believe we are not now and we do not anticipate becoming a USRPHC. However, because the determination of whether we are a USRPHC at any time depends on the proportion of our assets, by fair market value, that consists of U.S. real property interests, there can be no assurance we are not now a USRPHC or we will not become one in the future. Even if we are or become a USRPHC, for so long as our common stock is "regularly traded," as defined by applicable Treasury Regulations, on an established securities market, sales of our common stock generally will not be subject to tax for non-U.S. holders that have held less than 5% of our common stock, actually or constructively, during the applicable statutory period.

### **Information Reporting and Backup Withholding**

Generally, we must report annually to the IRS and to each non-U.S. holder the amount of dividends and other distributions paid to the non-U.S. holder and the amount of tax, if any withheld with respect to

those distributions. Pursuant to applicable income tax treaties or other agreements, the IRS may make these reports available to tax authorities in the non-U.S. holder's country of residence.

In addition, a non-U.S. holder may be subject to information reporting requirements and backup withholding with respect to dividends paid on, and the proceeds of disposition of, shares of our common stock, unless, generally, the non-U.S. holder certifies under penalties of perjury (usually on IRS Form W-8BEN or W-8BEN-E) that the non-U.S. holder is not a U.S. person or otherwise establishes an exemption. The current backup withholding rate is 28%. Additional rules relating to information reporting requirements and backup withholding with respect to payments of the proceeds from the disposition of shares of our common stock are as follows:

- If the proceeds are paid to or through the United States office of a broker, the proceeds generally will be subject to backup withholding and information reporting, unless the non-U.S. holder certifies under penalties of perjury (usually on IRS Form W-8BEN or W-8BEN-E) that the non-U.S. holder is not a U.S. person or otherwise establishes an exemption.
- If the proceeds are paid to or through a non-U.S. office of a broker that is not a U.S. person and is not a foreign person with certain specified U.S. connections, which we refer to below as a "U.S.-related person," information reporting and backup withholding generally will not apply.
- If the proceeds are paid to or through a non-U.S. office of a broker that is a U.S. person or a U.S.-related person, the proceeds generally will be subject to information reporting (but not to backup withholding), unless the non-U.S. holder certifies under penalties of perjury (usually on IRS Form W-8BEN or W-8BEN-E) that the non-U.S. holder is not a U.S. person.

Backup withholding is not a tax. Any amounts withheld from a non-U.S. holder under the backup withholding rules may be allowed as a refund or a credit against the non-U.S. holder's U.S. federal income tax liability, provided that the non-U.S. holder timely furnishes the required information to the IRS.

### **Foreign Account Tax Compliance Act**

Legislation enacted in 2010 and related guidance, commonly referred to as "FATCA," will impose withholding taxes on certain types of payments made to "foreign financial institutions" and other non-U.S. entities after June 30, 2014 (or, as discussed below, after later dates) unless those institutions and entities meet additional certification, information reporting and other requirements. The legislation will generally impose a 30% withholding tax on dividends on, or gross proceeds from the sale or other disposition of, our common stock paid to a foreign financial institution unless the foreign financial institution enters into an agreement with the U.S. Treasury to, among other things, (i) undertake to identify accounts held by certain U.S. persons (including certain equity and debt holders of such institution) or by U.S.-owned foreign entities, (ii) annually report certain information about such accounts, and (iii) withhold 30% on payments to account holders whose actions prevent it from complying with these reporting and other requirements. In addition, subject to certain exceptions, the legislation will impose a 30% withholding tax on the same types of payments to a foreign entity that is not a foreign financial institution unless the entity certifies that it does not have any substantial U.S. owners (which generally include any U.S. persons who directly or indirectly own more than 10% of the entity) or furnishes identifying information regarding each such substantial U.S. owner. These withholding taxes will be imposed on dividends paid on our common stock after June 30, 2014 (or, in certain cases, after later dates), and on gross proceeds from sales or other dispositions of our common stock after December 31, 2016. Withholding under FATCA generally will not be reduced or limited by bilateral income tax treaties. However, a non-U.S. holder may be exempt from FATCA withholding under an applicable intergovernmental agreement between the United States and a foreign government relating to the implementation of FATCA, provided that the non-U.S. holder and the foreign government comply with the terms of the agreement.

## UNDERWRITING

Subject to the terms and conditions set forth in an underwriting agreement, each of the underwriters named below has severally agreed to purchase from us the aggregate number of shares of common stock set forth opposite their respective names below:

<u>Underwriters</u>	<u>Number of Shares</u>
Stifel, Nicolaus & Company, Incorporated	
JMP Securities LLC	
Robert W. Baird & Co. Incorporated	
Oppenheimer & Co. Inc.	
Total	

The underwriting agreement provides that the obligations of the several underwriters are subject to various conditions, including approval of legal matters by counsel. The nature of the underwriters' obligations commits them to purchase and pay for all of the shares of common stock listed above if any are purchased. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

### Option to Purchase Additional Shares

We have granted the underwriters an option, exercisable for 30 days from the date of this prospectus, to purchase up to a total of \_\_\_\_\_ additional shares of our common stock from us, at the initial public offering price, less the underwriting discounts and commissions payable by us, as set forth on the cover page of this prospectus. If the underwriters exercise this option in whole or in part, then each of the underwriters will be separately committed, subject to the conditions described in the underwriting agreement, to purchase the additional shares of our common stock in proportion to their respective commitments set forth in the table above. We will pay the expenses associated with the exercise of the option to purchase additional shares.

### Determination of Offering Price

Prior to this offering, there has been no public market for our common stock. The initial public offering price will be determined through negotiations between us and Stifel, Nicolaus & Company, Incorporated and JMP Securities LLC, as the representatives of the several underwriters. In addition to prevailing market conditions, the factors to be considered in determining the initial public offering price will include:

- the information set forth in this prospectus and otherwise available to the representatives;
- our history and prospects, including our past and present financial performance and our prospects for future earnings;
- the history and prospects of companies in our industry;
- prior offerings of those companies;
- our capital structure;
- an assessment of our management and their experience;
- general conditions of the securities markets at the time of the offering; and
- other factors as we deem relevant.

We cannot assure you that an active or orderly trading market will develop for our common stock or that our common stock will trade in the public markets subsequent to this offering at or above the initial public offering price.



## Commissions and Discounts

The underwriters propose to offer the shares of common stock directly to the public at the initial public offering price set forth on the cover page of this prospectus, and at this price less a concession not in excess of \$ \_\_\_\_\_ per share of common stock to other securities dealers. After this offering, the offering price, concessions, and other selling terms may be changed by the underwriters. Our common stock is offered subject to receipt and acceptance by the underwriters and to certain other conditions, including the right to reject orders in whole or in part.

The following table summarizes the compensation to be paid to the underwriters by us and the proceeds, before expenses, payable to us. Such amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

	Total		
	Per Share	No Exercise	Full Exercise
Public offering price	\$ _____	\$ _____	\$ _____
Underwriting discounts and commissions	\$ _____	\$ _____	\$ _____
Proceeds, before expenses, to us	\$ _____	\$ _____	\$ _____

Pursuant to the terms of the underwriting agreement, we have also agreed to reimburse the underwriters for certain expenses, including reasonable fees and expenses of counsel, relating to certain aspects of this offering that will not exceed \$ \_\_\_\_\_.

We estimate that the total expenses of the offering payable by us, including registration, filing and listing fees, printing fees and legal and accounting expenses, but excluding underwriting discounts and commissions, will be approximately \$ \_\_\_\_\_.

## Indemnification of Underwriters

We will indemnify the underwriters against some civil liabilities, including liabilities under the Securities Act. If we are unable to provide this indemnification, we will contribute to payments the underwriters may be required to make in respect of those liabilities.

## No Sale of Similar Securities

We and each of our directors and executive officers and holders of substantially all of our outstanding capital stock, options and warrants prior to this offering have agreed, subject to specified exceptions, that we and they will not, for a period of 180 days after the date of this prospectus, without the prior written consent of each of Stifel, Nicolaus & Company, Incorporated and JMP Securities LLC, directly or indirectly:

- offer, sell, contract to sell (including any short sale), pledge, hypothecate transfer, establish an open "put equivalent position" within the meaning of Rule 16a-1(h) under the Exchange Act, grant any option, right or warrant for the sale of, purchase any option or contract to sell, sell any option or contract to purchase;
- otherwise encumber, dispose of or transfer, or grant any rights with respect to, directly or indirectly, any shares of our common stock or securities convertible into or exchangeable or exercisable for any shares of our common stock, enter into a transaction which would have the same effect, or enter into any swap, hedge or other arrangement that transfers, in whole or in part, any of the economic consequences of ownership of our common stock, whether any such aforementioned transaction is to be settled by delivery of our common stock or such other securities, in cash or otherwise; or
- publicly disclose the intention to do any of the foregoing.

Stifel, Nicolaus & Company, Incorporated and JMP Securities LLC may, in their sole discretion and at any time or from time to time before the termination of the 180-day period, release all or any portion of

the securities subject to lock-up agreements. There are no existing agreements between the underwriters and any of our stockholders who will execute a lock-up agreement providing consent to the sale of shares prior to the expiration of the restricted period.

### **NASDAQ Market Listing**

We have applied to list our common stock on the NASDAQ Global Market under the symbol "PRTO."

### **Short Sales, Stabilizing Transactions, and Penalty Bids**

In order to facilitate this offering, persons participating in this offering may engage in transactions that stabilize, maintain, or otherwise affect the price of our common stock during and after this offering. Specifically, the underwriters may engage in the following activities in accordance with the rules of the SEC.

*Short sales.* Short sales involve the sales by the underwriters of a greater number of shares than they are required to purchase in the offering. Covered short sales are short sales made in an amount not greater than the underwriters' over-allotment option to purchase additional shares from us in this offering. The underwriters may close out any covered short position by either exercising their over-allotment option to purchase shares or purchasing shares in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the over-allotment option. Naked short sales are any short sales in excess of such over-allotment option. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market after pricing that could adversely affect investors who purchase in this offering.

*Stabilizing transactions.* The underwriters may make bids for or purchases of the shares for the purpose of pegging, fixing, or maintaining the price of the shares, so long as stabilizing bids do not exceed a specified maximum.

*Penalty bids.* If the underwriters purchase shares in the open market in a stabilizing transaction or syndicate covering transaction, they may reclaim a selling concession from the underwriters and selling group members who sold those shares as part of this offering. Stabilization and syndicate covering transactions may cause the price of the shares to be higher than it would be in the absence of these transactions. The imposition of a penalty bid might also have an effect on the price of the shares if it discourages resales of the shares.

The transactions above may occur on the NASDAQ Global Market or otherwise. Neither we nor the underwriters make any representation or prediction as to the effect that the transactions described above may have on the price of the shares. If these transactions are commenced, they may be discontinued without notice at any time.

### **Discretionary Sales**

The underwriters have informed us that they do not expect to confirm sales of common stock offered by this prospectus to accounts over which they exercise discretionary authority without obtaining the specific approval of the account holder.

## **Electronic Distribution**

A prospectus in electronic format may be made available on the internet sites or through other online services maintained by one or more of the underwriters participating in this offering, or by their affiliates. Other than the prospectus in electronic format, the information on any underwriter's web site and any information contained in any other web site maintained by an underwriter is not part of the prospectus or the registration statement of which this prospectus forms a part, has not been approved and/or endorsed by us or any underwriter in its capacity as underwriter and should not be relied upon by investors.

## **Relationships**

The underwriters and their respective affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, principal investment, hedging, financing and brokerage activities. Certain of the underwriters and their affiliates may in the future from time to time provide, investment banking and other financing and banking services to us, for which they may receive, customary fees and reimbursement for their expenses. In the ordinary course of their various business activities, the underwriters and their respective affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers and may at any time hold long and short positions in such securities and instruments. Such investment and securities activities may involve our securities and instruments.

## **Notice to Prospective Investors in the European Economic Area**

In relation to each member state of the European Economic Area that has implemented the Prospectus Directive (each, a relevant member state), with effect from and including the date on which the Prospectus Directive is implemented in that relevant member state (the relevant implementation date), an offer of securities described in this prospectus may not be made to the public in that relevant member state other than:

- to any legal entity that is authorized or regulated to operate in the financial markets or, if not so authorized or regulated, whose corporate purpose is solely to invest in securities;
- to any legal entity that has two or more of (1) an average of at least 250 employees during the last financial year; (2) a total balance sheet of more than €43,000,000 and (3) an annual net turnover of more than €50,000,000, as shown in its last annual or consolidated accounts;
- to fewer than 100 natural or legal persons (other than qualified investors as defined in the Prospectus Directive) subject to obtaining the prior consent of the representatives; or
- in any other circumstances that do not require the publication of a prospectus pursuant to Article 3 of the Prospectus Directive,

provided that no such offer of securities shall require us or any underwriter to publish a prospectus pursuant to Article 3 of the Prospectus Directive. For purposes of this provision, the expression an "offer of securities to the public" in any relevant member state means the communication in any form and by any means of sufficient information on the terms of the offer and the securities to be offered so as to enable an investor to decide to purchase or subscribe the securities, as the expression may be varied in that member state by any measure implementing the Prospectus Directive in that member state, and the expression "Prospectus Directive" means Directive 2003/71/EC and includes any relevant implementing measure in each relevant member state.

We have not authorized and do not authorize the making of any offer of securities through any financial intermediary on their behalf, other than offers made by the underwriters with a view to the final placement of the securities as contemplated in this prospectus. Accordingly, no purchaser of the securities,

other than the underwriters, is authorized to make any further offer of the securities on behalf of us or the underwriters.

#### **Notice to Prospective Investors in the United Kingdom**

This prospectus is only being distributed to, and is only directed at, persons in the United Kingdom that are qualified investors within the meaning of Article 2(1)(e) of the Prospectus Directive (Qualified Investors) that are also (1) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005 (the Order) or (2) high net worth entities, and other persons to whom it may lawfully be communicated, falling within Article 49(2)(a) to (d) of the Order (all such persons together being referred to as relevant persons). This prospectus and its contents are confidential and should not be distributed, published or reproduced (in whole or in part) or disclosed by recipients to any other persons in the United Kingdom. Any person in the United Kingdom that is not a relevant person should not act or rely on this document or any of its contents.

#### **Notice to Prospective Investors in France**

This prospectus has not been prepared in the context of a public offering of financial securities in France within the meaning of Article L.411-1 of the French Code Monétaire et Financier and Title I of Book II of the Règlement Général of the Autorité des marchés financiers, or the AMF, and therefore has not been and will not be filed with the AMF for prior approval or submitted for clearance to the AMF. Consequently, the shares of our common stock may not be, directly or indirectly, offered or sold to the public in France and offers and sales of the shares of our common stock may only be made in France to qualified investors (investisseurs qualifiés) acting for their own, as defined in and in accordance with Articles L.411-2 and D.411-1 to D.411-4, D.734-1, D.744-1, D.754-1 and D.764-1 of the French Code Monétaire et Financier. Neither this prospectus nor any other offering material may be released, issued or distributed to the public in France or used in connection with any offer for subscription or sale of the shares of our common stock to the public in France. The subsequent direct or indirect retransfer of the shares of our common stock to the public in France may only be made in compliance with Articles L.411-1, L.411-2, L.412-1 and L.621-8 through L.621-8-3 of the French Code Monétaire et Financier.

#### **Notice to Prospective Investors in Germany**

Each person who is in possession of this prospectus is aware of the fact that no German securities prospectus (wertpapierprospekt) within the meaning of the securities prospectus act (wertpapier-prospektgesetz, the "act") of the federal republic of Germany has been or will be published with respect to the shares of our common stock. In particular, each underwriter has represented that it has not engaged and has agreed that it will not engage in a public offering in the federal republic of Germany (öffentliches angebot) within the meaning of the act with respect to any of the shares of our common stock otherwise than in accordance with the act and all other applicable legal and regulatory requirements.

#### **Notice to Prospective Investors in Switzerland**

The securities which are the subject of the offering contemplated by this prospectus may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange, or SIX, or on any other stock exchange or regulated trading facility in Switzerland. This prospectus has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. None of this prospectus or any other offering or marketing material relating to the securities or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

None of this prospectus or any other offering or marketing material relating to the offering, us or the securities have been or will be filed with or approved by any Swiss regulatory authority. In particular, this prospectus will not be filed with, and the offer of securities will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA and the offer of securities has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes, or CISA. The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of the securities.

#### **Notice to Prospective Investors in the Netherlands**

The offering of the shares of our common stock is not a public offering in The Netherlands. The shares of our common stock may not be offered or sold to individuals or legal entities in The Netherlands unless (1) a prospectus relating to the offer is available to the public, which has been approved by the Dutch Authority for the Financial Markets (Autoriteit Financiële Markten) or by the competent supervisory authority of another state that is a member of the European Union or party to the Agreement on the European Economic Area, as amended or (2) an exception or exemption applies to the offer pursuant to Article 5:3 of The Netherlands Financial Supervision Act (Wet op het financieel toezicht) or Article 53 paragraph 2 or 3 of the Exemption Regulation of the Financial Supervision Act, for instance due to the offer targeting exclusively "qualified investors" (gekwalificeerde beleggers) within the meaning of Article 1:1 of The Netherlands Financial Supervision Act.

#### **Notice to Prospective Investors in Japan**

The underwriters will not offer or sell any of the shares of our common stock directly or indirectly in Japan or to, or for the benefit of, any Japanese person or to others, for re-offering or re-sale directly or indirectly in Japan or to any Japanese person, except in each case pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the Financial Instruments and Exchange Law of Japan and any other applicable laws and regulations of Japan. For purposes of this paragraph, "Japanese person" means any person resident in Japan, including any corporation or other entity organized under the laws of Japan.

#### **Notice to Prospective Investors in Hong Kong**

The underwriters and each of their affiliates have not (1) offered or sold, and will not offer or sell, in Hong Kong, by means of any document, any shares of our common stock other than (a) to "professional investors" within the meaning of the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance or (b) in other circumstances which do not result in the document being a "prospectus" as defined in the Companies Ordinance (Cap. 32) of Hong Kong or which do not constitute an offer to the public within the meaning of that Ordinance; and (2) issued or had in its possession for the purposes of issue, and will not issue or have in its possession for the purposes of issue, whether in Hong Kong or elsewhere any advertisement, invitation or document relating to the shares of our common stock which is directed at, or the contents of which are likely to be accessed or read by, the public in Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to the shares of our common stock which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" within the meaning of the Securities and Futures Ordinance and any rules made under that Ordinance. The contents of this document have not been reviewed by any regulatory authority in Hong Kong. You are advised to exercise caution in relation to the offer. If you are in any doubt about any of the contents of this document, you should obtain independent professional advice.

#### **Notice to Prospective Investors in Singapore**

This document has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this document and any other document or material in connection with the offer or sale, or

invitation for subscription or purchase, of shares of our common stock may not be circulated or distributed, nor may shares of our common stock be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (1) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore, or the Securities and Futures Act, (2) to a relevant person, or any person pursuant to Section 275(1A), and in accordance with the conditions, specified in Section 275 of the Securities and Futures Act or (3) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the Securities and Futures Act.

Where shares of our common stock are subscribed or purchased under Section 275 by a relevant person which is:

- a) a corporation (which is not an accredited investor) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or
- b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary is an accredited investor, shares, debentures and units of shares and debentures of that corporation or the beneficiaries' rights and interest in that trust shall not be transferable for six months after that corporation or that trust has acquired the shares of our common stock under Section 275 except:
  - 1) to an institutional investor or to a relevant person, or to any person pursuant to an offer that is made on terms that such rights or interest are acquired at a consideration of not less than \$200,000 (or its equivalent in a foreign currency) for each transaction, whether such amount is to be paid for in cash or by exchange of securities or other assets;
  - 2) where no consideration is given for the transfer; or
  - 3) by operation of law.

## LEGAL MATTERS

The validity of the shares of common stock offered hereby will be passed upon for us by Bingham McCutchen LLP. Certain legal matters in connection with this offering will be passed upon for the underwriters by Ropes & Gray LLP.

## EXPERTS

The financial statements of Proteon Therapeutics, Inc. at December 31, 2012 and 2013 and for the years then ended, appearing in this prospectus and registration statement, have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon appearing elsewhere herein, and are included in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

## WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-1 (including exhibits, schedules, and amendments) under the Securities Act with respect to the shares of common stock offered by this prospectus. This prospectus does not contain all the information set forth in the registration statement. For further information about us and the shares of common stock to be sold in this offering, you should refer to the registration statement. Statements contained in this prospectus relating to the contents of any contract, agreement or other document are not necessarily complete and are qualified in all respects by the complete text of the applicable contract, agreement or other document, a copy of which has been filed as an exhibit to the registration statement. Whenever this prospectus refers to any contract, agreement, or other document, you should refer to the exhibits that are a part of the registration statement for a copy of the contract, agreement, or document.

You may read and copy all or any portion of the registration statement or any other information we file at the SEC's public reference room at 100 F Street, N.E., Room 1580, Washington, D.C. 20549. You can request copies of these documents, upon payment of a duplicating fee, by writing to the SEC. Please call the SEC at 1-800-SEC-0330 for further information about the operation of the public reference rooms. Our SEC filings, including the registration statement, are also available to you on the SEC's Website (<http://www.sec.gov>).

Upon completion of this offering, we will become subject to the information and periodic reporting requirements of the Exchange Act. Under the Exchange Act, we will file annual, quarterly and current reports, as well as proxy statements and other information with the SEC. These periodic reports, proxy statements, and other information will be available for inspection and copying at the SEC's Public Reference Room and the website of the SEC referred to above.

**Proteon Therapeutics, Inc.**

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**Proteon Therapeutics, Inc.**

**Report of Independent Registered Public Accounting Firm**

The Board of Directors and Shareholders of Proteon Therapeutics, Inc.

We have audited the accompanying balance sheets of Proteon Therapeutics, Inc. as of December 31, 2012 and 2013, and the related statements of operations and comprehensive loss, redeemable convertible preferred stock and stockholders' deficit, and cash flows for the years then ended. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. We were not engaged to perform an audit of the Company's internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of Proteon Therapeutics, Inc. at December 31, 2012 and 2013, and the results of its operations and its cash flows for the years then ended, in conformity with U.S. generally accepted accounting principles.

/s/ Ernst & Young LLP

Boston, MA  
June 25, 2014

Proteon Therapeutics, Inc.

Balance Sheets

(in thousands, except share and per share data)

	December 31,		March 31, 2014	
	2012	2013	Actual	Pro forma (unaudited)
<b>Assets</b>				
Current assets:				
Cash and cash equivalents	\$ 2,409	\$ 2,793	\$ 3,586	\$ 3,586
Available-for-sale investments	5,062	2,359	—	—
Prepaid expenses	152	61	240	240
Other current assets	41	78	125	125
Short-term deposits	39	39	39	39
Total current assets	7,703	5,330	3,990	3,990
Property and equipment, net	79	62	55	55
Deferred tax asset	—	267	—	—
Total assets	<u>\$ 7,782</u>	<u>\$ 5,659</u>	<u>\$ 4,045</u>	<u>\$ 4,045</u>
<b>Liabilities, redeemable convertible preferred stock and stockholders' deficit</b>				
Current liabilities:				
Convertible notes, including accrued interest payable of \$0 and \$112 as of December 31, 2012 and 2013, \$198 (unaudited) as of March 31, 2014, and \$0 (unaudited) pro forma	\$ —	\$ 3,727	\$ 4,536	\$ —
Derivative liability	—	1,443	1,512	—
Accounts payable	469	399	348	348
Accrued expenses	735	984	1,624	1,624
Deferred tax liability	—	267	—	—
Current portion of deferred revenue from sale of option to acquire company	—	2,948	2,948	2,948
Total current liabilities	1,204	9,768	10,968	4,920
Deferred revenue from sale of option to acquire company	2,948	—	—	—
Total liabilities	4,152	9,768	10,968	4,920
Commitments and contingencies (Note 8)				
Redeemable convertible preferred stock:				
Series A redeemable convertible preferred stock, \$0.001 par value, 22,638,465 shares authorized, issued, and outstanding at December 31, 2012, December 31, 2013, and March 31, 2014 (unaudited); no shares issued and outstanding pro forma (unaudited); aggregate liquidation preference of \$22,638 at December 31, 2012, 2013 and March 31, 2014 (unaudited) and none pro forma (unaudited)	32,633	34,230	34,624	—
Series A-1 redeemable convertible preferred stock, \$0.001 par value, 10,909,091 shares authorized, issued, and outstanding at December 31, 2012, December 31, 2013 and March 31, 2014 (unaudited); and no shares issued and outstanding pro forma (unaudited); aggregate liquidation preference of \$12,000 at December 31, 2012, December 31, 2013, and March 31, 2014 (unaudited) and none pro forma (unaudited)	16,526	17,374	17,583	—
Series B redeemable convertible preferred stock, \$0.001 par value, 20,754,461 shares authorized, issued, and outstanding at December 31, 2012, December 31, 2013, and March 31, 2014 (unaudited); no shares issued and outstanding pro forma (unaudited); aggregate liquidation preference of \$23,867 at December 31, 2012, December 31, 2013, and March 31, 2014 (unaudited) and none pro forma (unaudited)	24,926	27,401	28,014	—
Series C redeemable convertible preferred stock, \$0.001 par value, 17,550,758 shares authorized, 13,202,932 issued, and outstanding at December 31, 2012, December 31, 2013, and March 31, 2014 (unaudited); no shares issued and outstanding pro forma (unaudited); aggregate liquidation preference of \$15,183 at December 31, 2012, December 31, 2013, and March 31, 2014 (unaudited) and none pro forma (unaudited)	16,201	17,400	17,696	—
Stockholders' deficit:				
Common stock, \$0.001 par value, 100,370,203 shares authorized at December 31, 2012, December 31, 2013, March 31, 2014 (unaudited) and pro forma (unaudited); 3,659,790, 3,807,356 and 3,811,106 issued and outstanding at December 31, 2012, December 31, 2013, and March 31, 2014, respectively, and 75,260,798 shares issued and outstanding pro forma (unaudited)	4	4	4	76
Additional paid-in capital	—	—	—	102,381
Accumulated deficit	(86,661)	(100,518)	(104,844)	(103,332)
Accumulated other comprehensive income	1	—	—	—
Total stockholders' deficit	(86,656)	(100,514)	(104,840)	(875)
Total liabilities, redeemable convertible preferred stock and stockholders' deficit	<u>\$ 7,782</u>	<u>\$ 5,659</u>	<u>\$ 4,045</u>	<u>\$ 4,045</u>

See accompanying notes to financial statements.

Proteon Therapeutics, Inc.

Statements of Operations and Comprehensive Loss

(in thousands, except share and per share data)

	Year Ended December 31,		Three Months Ended March 31,	
	2012	2013	2013	2014
	(unaudited)			
Operating expenses:				
Research and development	\$ 5,907	\$ 3,994	\$ 1,134	\$ 1,189
General and administrative	2,089	3,128	737	744
Total operating expenses	7,996	7,122	1,871	1,933
Loss from operations	(7,996)	(7,122)	(1,871)	(1,933)
Other income (expense):				
Investment income	20	4	2	—
Interest expense	—	(861)	—	(828)
Other income (expense)	6	67	4	(70)
Total other income (expense)	26	(790)	6	(898)
Net loss	\$ (7,970)	\$ (7,912)	\$ (1,865)	\$ (2,831)
Unrealized loss on available-for-sale investments	(5)	(1)	—	—
Comprehensive loss	\$ (7,975)	\$ (7,913)	\$ (1,865)	\$ (2,831)
Reconciliation of net loss to net loss attributable to common stockholders:				
Net loss	\$ (7,970)	\$ (7,912)	\$ (1,865)	\$ (2,831)
Accretion of redeemable convertible preferred stock to redemption value	(6,133)	(6,119)	(1,512)	(1,512)
Net loss attributable to common stockholders	\$ (14,103)	\$ (14,031)	\$ (3,377)	\$ (4,343)
Net loss per share attributable to common stockholders—basic and diluted	\$ (3.85)	\$ (3.76)	\$ (0.92)	\$ (1.14)
Weighted-average number of common shares used in net loss per share attributable to common stockholders—basic and diluted	3,659,790	3,732,436	3,659,790	3,811,014
Pro forma net loss per share attributable to common stockholders—basic and diluted (unaudited)		\$ (0.10)		\$ (0.03)
Pro forma weighted-average number of common shares used in net loss per share attributable to common stockholders—basic and diluted (unaudited)		72,457,068		75,186,284

See accompanying notes to financial statements

Statements of Redeemable Convertible Preferred Stock and Stockholders' Deficit

(in thousands, except share and per share data)

	Series A Redeemable Convertible Preferred Stock		Series A-1 Redeemable Convertible Preferred Stock		Series B Redeemable Convertible Preferred Stock		Series C Redeemable Convertible Preferred Stock		Common Stock			Accumulated Deficit	Accumulated Other Comprehensive Income	Total Stockholders' Deficit
	Shares	Amount	Shares	Amount	Shares	Amount	Shares	Amount	Shares	\$0.001 Par Value	Additional Paid-in Capital			
<b>Balance at December 31, 2011</b>	22,638,465	\$ 31,031	10,909,091	\$ 15,677	20,754,461	\$ 22,446	13,202,932	\$ 14,999	3,659,790	\$ 4	\$ —	(72,668)	\$ 5	(72,659)
Accretion of Series A, A-1, B and C redeemable convertible preferred stock to redemption value	—	1,602	—	849	—	2,480	—	1,202	—	—	(110)	(6,023)	—	(6,133)
Stock-based compensation expense	—	—	—	—	—	—	—	—	—	—	110	—	—	110
Unrealized gain (loss) on short term investments	—	—	—	—	—	—	—	—	—	—	—	—	(4)	(4)
Net loss	—	—	—	—	—	—	—	—	—	—	—	(7,970)	—	(7,970)
<b>Balance at December 31, 2012</b>	22,638,465	\$ 32,633	10,909,091	\$ 16,526	20,754,461	\$ 24,926	13,202,932	\$ 16,201	3,659,790	\$ 4	\$ —	(86,661)	\$ 1	(86,656)
Accretion of Series A, A-1, B and C redeemable convertible preferred stock to redemption value	—	1,597	—	848	—	2,475	—	1,199	—	—	(174)	(5,945)	—	(6,119)
Exercise of common stock options	—	—	—	—	—	—	—	—	147,566	—	19	—	—	19
Stock-based compensation expense	—	—	—	—	—	—	—	—	—	—	155	—	—	155
Unrealized gain (loss) on short term investments	—	—	—	—	—	—	—	—	—	—	—	—	(1)	(1)
Net loss	—	—	—	—	—	—	—	—	—	—	—	(7,912)	—	(7,912)
<b>Balance at December 31, 2013</b>	22,638,465	\$ 34,230	10,909,091	\$ 17,374	20,754,461	\$ 27,401	13,202,932	\$ 17,400	3,807,356	\$ 4	\$ —	(100,518)	\$ —	(100,514)
Accretion of Series A, A-1, B and C redeemable convertible preferred stock to redemption value	—	394	—	209	—	613	—	296	—	—	(17)	(1,495)	—	(1,512)
Exercise of common stock options	—	—	—	—	—	—	—	—	3,750	0	0	—	—	0
Stock-based compensation expense	—	—	—	—	—	—	—	—	—	—	17	—	—	17
Unrealized gain (loss) on short term investments	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Net loss	—	—	—	—	—	—	—	—	—	—	—	(2,831)	—	(2,831)
<b>Balance at March 31, 2014 (Unaudited)</b>	22,638,465	\$ 34,624	10,909,091	\$ 17,583	20,754,461	\$ 28,014	13,202,932	\$ 17,696	3,811,106	\$ 4	\$ —	(104,844)	\$ —	(104,840)
Conversion of redeemable convertible preferred stock into common stock (unaudited)	(22,638,465)	(34,624)	(10,909,091)	(17,583)	(20,754,461)	(28,014)	(13,202,932)	(17,696)	67,504,949	68	97,849	—	—	97,917
Conversion of convertible notes payable and accrued interest into common stock (unaudited)	—	—	—	—	—	—	—	—	3,944,743	4	4,532	1,512	—	6,048
<b>Pro forma balance at March 31, 2014 (Unaudited)</b>	—	\$ —	—	\$ —	—	\$ —	—	\$ —	75,260,798	\$ 76	\$ 102,381	\$ (103,332)	\$ —	(875)

See accompanying notes to financial statements.

Proteon Therapeutics, Inc.

Statements of Cash Flows

(in thousands)

	Year Ended December 31,		Three Months Ended March 31,	
	2012	2013	2013	2014
<b>Operating activities:</b>				
Net loss	\$ (7,970)	\$ (7,912)	\$ (1,865)	\$ (2,831)
Reconciliation of net loss to net cash used in operating activities:				
Depreciation	57	27	8	7
Amortization of premium/discount on available-for-sale securities	138	30	11	4
Gain on sale of fixed assets	(5)	(65)	(4)	—
Accretion of discount & debt issuance cost of convertible notes payable	—	749	—	741
Stock-based compensation	110	155	83	17
Change in fair value of derivative liability	—	(2)	—	69
Changes in:				
Prepaid expenses and other assets	320	71	35	(259)
Interest receivable	28	1	(5)	15
Accounts payable and accrued expenses	(912)	177	(51)	589
Accrued interest payable	—	112	—	86
Net cash used in operating activities	(8,234)	(6,657)	(1,788)	(1,562)
<b>Investing activities:</b>				
Purchases of available-for-sale investments	(8,658)	(3,878)	(1,510)	—
Proceeds from maturities of available for sale investments	16,075	6,550	3,300	2,355
Purchase of property and equipment	(67)	(10)	—	—
Sale of property and equipment	33	65	4	—
Deposits	(1)	—	—	—
Net cash provided by investing activities	7,382	2,727	1,794	2,355
<b>Financing activities:</b>				
Proceeds from issuance of convertible notes payable	—	4,339	—	—
Payments for debt issuance costs	—	(46)	—	—
Exercise of stock options	—	19	—	0
Early exercise of stock options	—	2	—	—
Repayments of note payable	(9)	—	—	—
Net cash (used in) provided by financing activities	(9)	4,314	—	0
(Decrease) increase in cash and cash equivalents	(861)	384	6	793
Cash and cash equivalents, beginning of period	3,270	2,409	2,409	2,793
Cash and cash equivalents, end of period	<u>\$ 2,409</u>	<u>\$ 2,793</u>	<u>\$ 2,415</u>	<u>\$ 3,586</u>
<b>Supplemental disclosure of non-cash investing and financing activities:</b>				
Accretion of redeemable convertible preferred stock to redemption value	<u>\$ 6,133</u>	<u>\$ 6,119</u>	<u>\$ 1,515</u>	<u>\$ 1,512</u>
Fair value of embedded derivative contained within convertible notes payable	<u>\$ —</u>	<u>\$ 1,445</u>	<u>\$ —</u>	<u>\$ 1,512</u>

See accompanying notes to financial statements.

Notes to Financial Statements

**1. Organization and operations**

**The Company**

Proteon Therapeutics, Inc. is an early-stage biopharmaceutical company engaged in the development of elastases to treat the growing medical needs of renal and vascular disease patients.

Proteon Therapeutics, LLC (the "LLC" or the "Predecessor") was organized in June 2001. Proteon Therapeutics, Inc., a Delaware corporation ("the Company"), was incorporated on March 24, 2006. Effective March 27, 2006, the Predecessor and the Company merged, with the Company being the surviving entity. During 2013, the Company formed a wholly-owned subsidiary, organized in the United Kingdom. As of March 31, 2014 there has been no activity other than its formation. Since the inception of the Predecessor on June 1, 2001, the Company has been primarily involved in research and development activities.

The Company devotes substantially all of its efforts to product research and development, initial market development and raising capital. The Company has not generated any product revenue related to its primary business purpose to date and is subject to a number of risks similar to those of other development stage companies, including dependence on key individuals, competition from other companies, the need for development of commercially viable products and the need to obtain adequate additional financing to fund the development of its product candidates. The Company is also subject to a number of risks similar to other companies in the life sciences industry, including regulatory approval of products, uncertainty of market acceptance of products, competition from substitute products and larger companies, the need to obtain additional financing, compliance with government regulations, protection of proprietary technology, dependence on third parties, product liability and dependence on key individuals.

The Company had an accumulated deficit of \$100.5 million as of December 31, 2013 and \$104.8 million as of March 31, 2014 (unaudited) and will require substantial additional capital to fund its research and development and ongoing operating expenses.

**Liquidity**

The Company believes that its cash, cash equivalents and short-term investments of approximately \$5.2 million as of December 31, 2013 and \$3.6 million as of March 31, 2014 (unaudited) as well as the additional capital raised in the subsequent financing (Note 15) will be sufficient to allow the Company to fund its operations at least beyond December 31, 2014; however, the Company may be required to raise additional capital or obtain financing from other sources to fund operations in the future. As the Company continues to incur losses, a transition to profitability is dependent upon the successful development, approval and commercialization of its product candidate and the achievement of a level of revenues adequate to support the Company's cost structure. The Company may never achieve profitability, and unless and until it does, the Company will continue to need to raise additional capital or obtain financing from other sources, such as strategic partnerships or other sources. There can be no assurances, however, that additional funding will be available on terms acceptable to the Company, or at all.

**2. Summary of Significant Accounting Policies**

**Basis of Presentation and Use of Estimates**

The accompanying financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America ("GAAP"). Any reference in these notes to applicable guidance is meant to refer to the authoritative United States generally accepted accounting principles as

Notes to Financial Statements (Continued)

**2. Summary of Significant Accounting Policies (Continued)**

found in the Accounting Standards Codification ("ASC") and Accounting Standards Update ("ASU") of the Financial Accounting Standards Board ("FASB"). The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. On an ongoing basis, the Company's management evaluates its estimates, which include, but are not limited to, estimates related to convertible notes, stock-based compensation expense, clinical trial accruals, and reported amounts of revenues and expenses during the reported period. The Company bases its estimates on historical experience and other market-specific or other relevant assumptions that it believes to be reasonable under the circumstances. Actual results may differ from those estimates or assumptions.

The Company utilizes significant estimates and assumptions in determining the fair value of its common stock ("Common Stock"). The Company utilized various valuation methodologies in accordance with the framework of the 2004 and 2013 American Institute of Certified Public Accountants Technical Practice Aids, *Valuation of Privately-Held Company Equity Securities Issued as Compensation*, to estimate the fair value of its Common Stock. Each valuation methodology includes estimates and assumptions that require the Company's judgment. These estimates and assumptions include a number of objective and subjective factors, including external market conditions affecting the biotechnology industry sector, the prices at which the Company sold shares of preferred stock, the superior rights and preferences of securities senior to the Company's Common Stock at the time and the likelihood of achieving a liquidity event, such as an initial public offering or a sale of the Company. Significant changes to the key assumptions used in the valuations could result in different fair values of Common Stock at each valuation date and materially affect the financial statements.

**Recent Accounting Pronouncements**

In June 2014, the FASB issued authoritative guidance regarding disclosure requirements of development stage companies in GAAP and International Financial Reporting Standards. This newly issued accounting standard removes all incremental financial reporting requirements, including inception-to-date information, for development stage entities. This guidance is effective for annual periods beginning after December 15, 2014. However, the Company early adopted this guidance effective with the publication of its 2013 financial statements.

**Unaudited Interim Financial Statements**

The accompanying balance sheet as of March 31, 2014, the statements of operations and comprehensive loss and statements of cash flows for the three months ended March 31, 2013 and 2014, the statement of redeemable convertible preferred stock and stockholders' deficit for the three months ended March 31, 2014 and the related information contained within the notes to the financial statements are unaudited. These interim financial statements have been prepared on the same basis as the annual audited financial statements and, in the opinion of management, reflect all adjustments, consisting of normal and recurring adjustments, necessary for the fair presentation of the Company's financial position at March 31, 2014 and results of its operations and its cash flows for the three months ended March 31, 2013 and 2014. The results for the three months ended March 31, 2014 are not necessarily indicative of results to be expected for the year ending December 31, 2014 or any other interim or future period.

Notes to Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

Unaudited Pro Forma Financial Information

On June 24, 2014, the Company's Board of Directors authorized the Company to file a registration statement with the Securities and Exchange Commission ("SEC") permitting the Company to sell shares of its Common Stock to the public. Upon the closing of a qualified (as defined in the Company's Articles of Incorporation) initial public offering ("IPO") or otherwise upon the election of the holders of the specified percentage of preferred stock, all of the Company's convertible notes plus accrued interest will convert into redeemable convertible preferred stock and the outstanding redeemable convertible preferred stock will automatically convert into Common Stock. The unaudited pro forma balance sheet and statement of redeemable convertible preferred stock and stockholders' (deficit) equity as of March 31, 2014 reflect the assumed conversion of: (a) all of the outstanding shares of Series A Redeemable Convertible Preferred Stock ("Series A Preferred Stock"), the Series A-1 Redeemable Convertible Preferred Stock ("Series A-1 Preferred Stock"), the Series B Redeemable Convertible Preferred Stock ("Series B Preferred Stock"), and the Series C Redeemable Convertible Preferred Stock ("Series C Preferred Stock") (collectively "Preferred Stock") and; (b) the outstanding convertible promissory notes issued in 2013 ("Convertible Notes") and associated accrued interest into shares of Common Stock and the reclassification of the related derivative liability to accumulated deficit. The conversion of the Convertible Notes has been reflected assuming the convertible promissory notes convert into shares of Series C Preferred Stock, and then immediately convert into Common Stock at a conversion price of \$1.15 per share. See Note 5 for further discussion of the Convertible Notes' conversion features. The assumed conversion and all pro forma financial information presented excludes the impact of the subsequent event financing (Note 15).

Unaudited pro forma net loss per share attributable to common stockholders is computed using the weighted-average number of common shares outstanding after giving effect to the conversion of all Preferred Stock and Convertible Notes and associated accrued interest into shares of the Common Stock as if such conversion had occurred at the beginning of the period presented, or the date of original issuance, if later, and excludes the accretion of Preferred Stock to its redemption value and interest expense of the Convertible Notes. Accordingly, the pro forma basic and diluted net loss per share attributable to common stockholders does not include the effects of the cumulative Preferred Stock dividends and extinguishment of Series B redeemable convertible Preferred Stock. As the years ended December 31, 2012 and December 31, 2013, the three months ended March 31, 2013 and 2014 (unaudited), resulted in net losses, there is no income allocation required under the two-class method or dilution attributed to pro forma weighted average shares outstanding in the calculation of pro forma diluted loss per share attributable to common stockholders.

As noted above, the unaudited pro forma information reflects the automatic conversion, at the closing of an IPO of the Company's Common Stock, of all Convertible Notes and associated accrued interest and outstanding shares of Preferred Stock into shares of Common Stock. The conversion of Preferred Stock has been reflected assuming shares of Series C Preferred Stock, Series B Preferred Stock, Series A-1 Preferred Stock and Series A Preferred Stock convert into shares of fully paid Common Stock reflecting a 1-to-1 conversion ratio. See Note 9 for further discussion of the Preferred Stock conversion features, as well as a discussion of the rights and preferences of the redeemable convertible Preferred Stock. The conversion of the Convertible Notes has been reflected assuming the convertible promissory notes convert into shares of Series C Preferred Stock at a conversion price of \$1.15 per share, and then immediately convert into Common Stock. See Note 5 for further discussion of the Convertible Notes conversion



Notes to Financial Statements (Continued)

**2. Summary of Significant Accounting Policies (Continued)**

features. The assumed conversion and all pro forma financial information presented excludes the impact of the subsequent event financing (Note 15).

**Segment Information**

Operating segments are defined as components of an enterprise about which separate discrete information is available for evaluation by the chief operating decision maker, or decision-making group, in deciding how to allocate resources and in assessing performance. The Company and the Company's chief operating decision maker view the Company's operations and manage its business in one operating segment, which is the business of developing and commercializing products for the treatment of renal and vascular disease. The Company operates in only one geographic segment.

**Cash and Cash Equivalents**

The Company considers all highly liquid investments with maturities of 90 days or less from the purchase date to be cash equivalents. Cash and cash equivalents are held in depository and money market accounts and are reported at fair value.

**Short-Term Investments**

The Company classifies its investments as available-for-sale and records such assets at estimated fair value in the balance sheets, with unrealized gains and losses, if any, reported as a component of other comprehensive income (loss) within the statements of operations and comprehensive loss and as a separate component of stockholders' (deficit) equity. The Company invests its excess cash balances primarily in government debt securities and money market funds with strong credit ratings and maturities of less than one year. There have been no realized gains and losses for the years ended December 31, 2012 and 2013 and for the three months ended March 31, 2013 and 2014 (unaudited).

At each balance sheet date, the Company assesses available-for-sale securities in an unrealized loss position to determine whether the unrealized loss is other-than-temporary. The Company considers factors including: the significance of the decline in value compared to the cost basis, underlying factors contributing to a decline in the prices of securities in a single asset class, the length of time the market value of the security has been less than its cost basis, the security's relative performance versus its peers, sector or asset class, expected market volatility and the market and economy in general. When the Company determines that a decline in the fair value below its cost basis is other-than-temporary, the Company recognizes an impairment loss in the year in which the other-than-temporary decline occurred. There have been no other-than-temporary declines in value of short-term investments for the years ended December 31, 2012 and 2013, the three months ended March 31, 2013 and 2014 (unaudited), as it is more likely than not the Company will hold the securities until maturity or a recovery of the cost basis.

**Concentrations of Credit Risk and Off-balance Sheet Risk**

Financial instruments that potentially subject the Company to concentrations of credit risk are primarily cash, cash equivalents and short-term investments. The Company's cash and cash equivalents are held in accounts with financial institutions that management believes are creditworthy. The Company's investment policy includes guidelines on the quality of the institutions and financial instruments and defines allowable investments that the Company believes minimizes the exposure to concentration of credit risk. These amounts at times may exceed federally insured limits. The Company has not experienced

Notes to Financial Statements (Continued)

**2. Summary of Significant Accounting Policies (Continued)**

any credit losses in such accounts and does not believe it is exposed to any significant credit risk on these funds. The Company has no financial instruments with off-balance sheet risk of loss.

**Deferred Public Offering Costs**

Deferred public offering costs, which primarily consist of direct, incremental legal and accounting fees relating to the IPO, are capitalized within other assets. The deferred issuance costs will be offset against IPO proceeds upon the consummation of the offering. In the event the offering is terminated, deferred offering costs will be expensed. The Company has incurred \$41,000 IPO costs as of March 31, 2014 (unaudited).

**Deferred Financing Costs**

Deferred financing costs related to the Convertible Notes as of December 31, 2013 were included in prepaid expenses and other current assets and have been fully amortized as of March 31, 2014 (unaudited) (Note 5). Deferred financing costs are amortized over the life of the related debt using the effective interest method. For the years ended December 31, 2012 and 2013, and for the three months ended March 31, 2013 and 2014 (unaudited), deferred financing costs of \$0, \$18, \$0 and \$18 thousand, respectively, were amortized to interest expense.

Direct and incremental costs incurred related to the issuance of the Series D Preferred Stock were recorded in other assets as of March 31, 2014 (unaudited). These deferred costs will be offset against the proceeds upon closing of the issuance of the Series D Preferred Stock (Note 15). As of March 31, 2014 (unaudited), the Company had incurred \$81,000 in Series D Preferred Stock issuance costs which were recorded in other assets.

**Fair Value of Financial Instruments**

The Company's financial instruments consist of cash and cash equivalents, short-term investments, accounts payable, accrued liabilities, Convertible Notes and features embedded in the Convertible Notes (see Note 5). The Company is required to disclose information on all assets and liabilities reported at fair value that enables an assessment of the inputs used in determining the reported fair values. FASB ASC Topic 820, *Fair Value Measurement and Disclosures*, established a hierarchy of inputs used in measuring fair value that maximizes the use of observable inputs and minimizes the use of unobservable inputs by requiring that the observable inputs be used when available. Observable inputs are inputs that market participants would use in pricing the financial instrument based on market data obtained from sources independent of the Company. Unobservable inputs are inputs that reflect the Company's assumptions about the inputs that market participants would use in pricing the financial instrument and are developed based on the best information available in the circumstances. The fair value hierarchy applies only to the valuation inputs used in determining the reported or disclosed fair value of the financial instruments and is not a measure of the investment credit quality. Fair value measurements are classified and disclosed in one of the following three categories:

- Level 1—Valuations based on unadjusted quoted prices in active markets for identical assets or liabilities that the Company has the ability to access at the measurement date.

Notes to Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

- Level 2—Valuations based on quoted prices for similar assets or liabilities in markets that are not active or for which all significant inputs are observable, either directly or indirectly.
- Level 3—Valuations that require inputs that reflect the Company's own assumptions that are both significant to the fair value measurement and unobservable.

To the extent that valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

Financial instruments measured at fair value on a recurring basis include cash equivalents, short-term investments (Note 3) and the derivative liability associated with the Convertible Notes (Note 5). The fair value of the derivative liability was determined based on Level 3 inputs as described in Note 5. An entity may elect to measure many financial instruments and certain other items at fair value at specified election dates. Subsequent unrealized gains and losses on items for which the fair value option has been elected will be reported in net loss. The Company did not elect to measure any additional financial instruments or other items at fair value. The Company is also required to disclose the fair value of financial instruments not carried at fair value. The carrying value of the Company's Convertible Notes approximates fair value considering their short-term maturity dates and considering that the stated interest rate is near current market rates for instruments with similar conversion and settlement features.

There have been no changes to the valuation methods utilized by the Company during the years ended December 31, 2012 and 2013, the three months ended March 31, 2013 and 2014 (unaudited). The Company evaluates transfers between levels at the end of each reporting period. There were no transfers of financial instruments between levels during the years ended December 31, 2012 and 2013, the three months ended March 31, 2013 and 2014 (unaudited).

**Derivative Instruments**

The Company occasionally issues financial instruments in which a derivative instrument is "embedded". Upon issuing the financial instrument, the Company assesses whether the economic characteristics of the embedded derivative are clearly and closely related to the economic characteristics of the remaining component of the financial instrument (i.e., the host contract) and whether a separate, non-embedded instrument with the same terms as the embedded instrument would meet the definition of a derivative instrument. When it is determined that (1) the embedded derivative possesses economic characteristics that are not clearly and closely related to the economic characteristics of the host contract and (2) a separate, stand-alone instrument with the same terms would qualify as a derivative instrument, the embedded derivative is separated from the host contract and carried at fair value with any changes in fair value recorded in current period earnings.

In connection with the issuance of the Convertible Notes in September 2013, the Company identified certain embedded features which require separation under ASC 815, *Derivatives and Hedging* ("ASC 815"). See Note 5 for further discussion of these instruments.

## Notes to Financial Statements (Continued)

## 2. Summary of Significant Accounting Policies (Continued)

## Property and Equipment

Property and equipment is stated at cost, less accumulated depreciation. Maintenance and repairs that do not improve or extend the lives of the respective assets are expensed to operations as incurred. Upon disposal, the related cost and accumulated depreciation is removed from the accounts and any resulting gain or loss is included in the results of operations. Depreciation is recorded using the straight-line method over the estimated useful lives of the respective assets, which are as follows:

<u>Asset</u>	<u>Estimated Useful Life</u>
Computer equipment and software	3 years
Furniture, fixtures, and other	5 years
Laboratory equipment	7 years

## Revenue

In general, the Company recognizes revenue when all of the following criteria are met: persuasive evidence of arrangement exists; delivery has occurred or services have been rendered; the Company's price to the customer is fixed or determinable and collectability is reasonably assured.

## Research and Development Costs

Research and development costs are charged to expense as incurred in performing research and development activities. The costs include employee compensation costs, facilities and overhead, clinical study and related clinical manufacturing costs, regulatory and other related costs. Nonrefundable advanced payments for goods or services to be received in the future for use in research and development activities are deferred and capitalized. The capitalized amounts are expensed as the related goods are delivered or the services are performed.

## Stock-based compensation expense

The Company accounts for its stock-based compensation awards to employees and directors in accordance with FASB ASC Topic 718, *Compensation-Stock Compensation* ("ASC 718"). ASC 718 requires all stock-based payments to employees, including grants of employee stock options and restricted stock, to be recognized in the statements of operations and comprehensive loss based on their grant date fair values. Compensation expense related to awards to employees is recognized on a straight-line basis based on the grant date fair value over the associated service period of the award, ASC 718 which is generally the vesting term. Share-based payments issued to non-employees are recorded at their fair values and are periodically revalued as the equity instruments vest and are recognized as expense over the related service period in accordance with the provisions of ASC 718 and FASB ASC Topic 505, *Equity*, and are expensed using an accelerated attribution model.

The Company estimates the fair value of its stock options using the Black-Scholes option pricing model, which requires the input of subjective assumptions, including (a) the expected stock price volatility, (b) the expected term of the award, (c) the risk-free interest rate, (d) expected dividends and (e) the estimated fair value of its Common Stock on the measurement date. Due to the lack of a public market for the trading of its Common Stock and a lack of company specific historical and implied volatility data, the Company has based its estimate of expected volatility on the historical volatility of a group of similar

## Notes to Financial Statements (Continued)

**2. Summary of Significant Accounting Policies (Continued)**

companies that are publicly traded. When selecting these public companies on which it has based its expected stock price volatility, the Company selected companies with comparable characteristics to it, including enterprise value, risk profiles, position within the industry and with historical share price information sufficient to meet the expected term of the stock based awards. The Company computes historical volatility data using the daily closing prices for the selected companies' shares during the equivalent period of the calculated expected term of the stock-based awards. The Company will continue to apply this process until a sufficient amount of historical information regarding the volatility of its own stock price becomes available. Due to the lack of Company specific historical option activity, the Company has estimated the expected term of its employee stock options using the "simplified" method, whereby, the expected term equals the arithmetic average of the vesting term and the original contractual term of the option. The expected term for nonemployee awards is the remaining contractual term of the option. The risk-free interest rates are based on the U.S. Treasury securities with a maturity date commensurate with the expected term of the associated award. The Company has never paid, and does not expect to pay dividends in the foreseeable future. Refer to "Note 2," "*Basis of presentation and use of estimates*," for a discussion of the Company's estimated fair value of its Common Stock.

The Company is also required to estimate forfeitures at the time of grant and revise those estimates in subsequent periods if actual forfeitures differ from its estimates. The Company uses historical data to estimate forfeitures and records stock-based compensation expense only for those awards that are expected to vest. To the extent that actual forfeitures differ from the Company's estimates, the differences are recorded as a cumulative adjustment in the period the estimates were revised. Stock-based compensation expense recognized in the financial statements is based on awards that are ultimately expected to vest.

**Income Taxes**

Income taxes are recorded in accordance with FASB ASC Topic 740, "Income Taxes" ("ASC 740"), which provides for deferred taxes using an asset and liability approach. Under this method, deferred tax assets and liabilities are determined based on the difference between the financial reporting and tax reporting basis of assets and liabilities and are measured using enacted tax rates and laws that are expected to be in effect when the differences are expected to reverse. Valuation allowances are provided if, based upon the weight of available evidence, it is more likely than not that some or all of the deferred tax assets will not be realized. The Company has evaluated available evidence and concluded that the Company may not realize the benefit of its deferred tax assets; therefore a valuation allowance has been established for the full amount of the deferred tax assets.

The Company accounts for uncertain tax positions in accordance with the provisions of ASC 740. When uncertain tax positions exist, the Company recognizes the tax benefit of tax positions to the extent that the benefit will more likely than not be realized. The determination as to whether the tax benefit will more likely than not be realized is based upon the technical merits of the tax position as well as consideration of the available facts and circumstances. As of December 31, 2012 and 2013, and March 31, 2014 (unaudited), the Company does not have any significant uncertain tax positions. The Company's practice is to recognize interest and/or penalties related to income tax matters in income tax expense. See Note 13 for further details.

Notes to Financial Statements (Continued)

2. Summary of Significant Accounting Policies (Continued)

Net loss per share attributable to common stockholders

Basic net loss per share attributable to common stockholders is calculated by dividing net loss attributable to common stockholders by the weighted average shares outstanding during the period, without consideration for Common Stock equivalents. Net loss attributable to common stockholders is calculated by adjusting the net loss of the Company for cumulative preferred stock dividends and accretion of preferred stock issuance costs. During periods of income, the Company allocates participating securities a proportional share of income determined by dividing total weighted average participating securities by the sum of the total weighted average common shares and participating securities (the "two class method"). The Company's redeemable convertible preferred stock participates in any dividends declared by the Company and are therefore considered to be participating securities. Participating securities have the effect of diluting both basic and diluted earnings per share during periods of income. During periods of loss, the Company allocates no loss to participating securities because they have no contractual obligation to share in the losses of the Company. Diluted net loss per share attributable to common stockholders is calculated by adjusting weighted average shares outstanding for the dilutive effect of Common Stock equivalents outstanding for the period, determined using the treasury-stock and if-converted methods. For purposes of the diluted net loss per share attributable to common stockholders calculation, preferred stock, stock options, warrants and the Convertible Notes are considered to be Common Stock equivalents but have been excluded from the calculation of diluted net loss per share attributable to common stockholders, as their effect would be anti-dilutive for all periods presented. Therefore, basic and diluted net loss per share were the same for all periods presented.

Comprehensive loss

Comprehensive loss consists of net income or loss and changes in equity during a period from transactions and other events and circumstances generated from non-owner sources. The Company's net loss equals comprehensive loss, net of any changes in the unrealized gains and losses of the Company's short-term investments, for all periods presented.

Subsequent events

The Company considers events or transactions that occur after the balance sheet date but prior to the date the financial statements are available to be issued for potential recognition or disclosure in the financial statements. The Company has completed an evaluation of all subsequent events after the audited balance sheet date of December 31, 2013 through June 25, 2014 and after the unaudited balance sheet date of March 31, 2014 through June 25, 2014, the dates the financial statements were available to be issued, to ensure that this filing includes appropriate disclosure of events both recognized in the financial statements as of December 31, 2013 and March 31, 2014 (unaudited), and events which occurred subsequently but were not recognized in the financial statements. See Note 15 for further details concerning events subsequent to the balance sheet dates.

## Notes to Financial Statements (Continued)

## 3. Financial Instruments

Below is a summary of assets and liabilities measured at fair value as of December 31, 2012 and 2013, and March 31, 2014:

	As of December 31, 2012			Total
	Quoted Prices in Active Markets (Level 1)	Significant Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)	
(in thousands)				
<b>Financial assets</b>				
Cash equivalents	\$ 2,395	\$ —	\$ —	\$ 2,395
Government securities	5,062	—	—	5,062
Total	\$ 7,457	\$ —	\$ —	\$ 7,457
<b>Financial liabilities</b>				
Derivative liability	\$ —	\$ —	\$ —	\$ —
Total	\$ —	\$ —	\$ —	\$ —

	As of December 31, 2013			Total
	Quoted Prices in Active Markets (Level 1)	Significant Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)	
(in thousands)				
<b>Financial assets</b>				
Cash equivalents	\$ 2,781	\$ —	\$ —	\$ 2,781
Government securities	2,359	—	—	2,359
Total	\$ 5,140	\$ —	\$ —	\$ 5,140
<b>Financial liabilities</b>				
Derivative liability	\$ —	\$ —	\$ 1,443	\$ 1,443
Total	\$ —	\$ —	\$ 1,443	\$ 1,443

	As of March 31, 2014 (unaudited)			Total
	Quoted Prices in Active Markets (Level 1)	Significant Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)	
(in thousands)				
<b>Financial assets</b>				
Cash equivalents	\$ 3,581	\$ —	\$ —	\$ 3,581
Government securities	—	—	—	—
Total	\$ 3,581	\$ —	\$ —	\$ 3,581
<b>Financial liabilities</b>				
Derivative liability	\$ —	\$ —	\$ 1,512	\$ 1,512
Total	\$ —	\$ —	\$ 1,512	\$ 1,512

## Notes to Financial Statements (Continued)

## 3. Financial Instruments (Continued)

The Company's cash equivalents consist principally of money market funds. Short-term investments, consisting principally of government debt securities and money market funds, are classified as available-for-sale. Cash equivalents and short-term investments are stated at fair value and consist of Level 1 financial instruments in the fair value hierarchy. The Company determines the fair value of its debt security holdings based on pricing from a service provider. The service provider values the securities based on market prices from a variety of industry-standard independent data providers. Such market prices are quoted prices in active markets for identical assets (Level 1 inputs).

The derivative liability is considered Level 3 because its fair value measurement is based, in part, on significant inputs not observed in the market. The Company determined the fair value of the derivative liability as described in Note 5. Any reasonable changes in the assumptions used in the valuation could materially affect the financial results of the Company.

Available-for-sale securities at December 31, 2012 and 2013 consist of the following (in thousands):

	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
<b>December 31, 2012</b>				
Government securities				
(Due within 1 year)	\$ 5,061	\$ 1	\$ —	\$ 5,062
	<u>\$ 5,061</u>	<u>\$ 1</u>	<u>\$ —</u>	<u>\$ 5,062</u>
<b>December 31, 2013</b>				
Government securities				
(Due within 1 year)	\$ 2,359	\$ —	\$ —	\$ 2,359
	<u>\$ 2,359</u>	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 2,359</u>

There were no short-term or available-for-sale investments held by the Company at March 31, 2014 (unaudited).

## 4. Property and equipment, net

Property and equipment, net, consists of the following (in thousands):

	December 31,		March 31,
	2012	2013	2014 (unaudited)
Computer equipment and software	\$ 86	\$ 96	\$ 96
Furniture, fixtures, and other	85	84	84
Laboratory equipment	410	236	236
	581	416	416
Accumulated depreciation	(502)	(354)	(361)
Property and equipment, net	<u>\$ 79</u>	<u>\$ 62</u>	<u>\$ 55</u>

Depreciation expense for the years ended December 31, 2012 and 2013, and for the three months ended March 31, 2013 and 2014 (unaudited) was \$57,000, \$27,000, \$8,000 and \$7,000, respectively.



Notes to Financial Statements (Continued)

**4. Property and equipment, net (Continued)**

During 2013, the Company sold fully depreciated fixed assets with an original cost basis of \$0.2 million and a net book value of \$0, recognizing a gain on sale of \$0.1 million, of which, \$4,000 was recognized during the three months ended March 31, 2013. The Company did not sell or dispose of any fixed assets during 2012 or the three months ended March 31, 2014 (unaudited).

**5. Convertible Notes**

On April 29, 2013, the Company entered into a Convertible Note Purchase Agreement ("the Note Agreement") with certain existing Preferred Stockholders. Under the terms of the Note Agreement, the Company had the option, but not the obligation, to borrow up to \$4.3 million from the issuance of the Convertible Notes, subject to meeting at least one of two pre-determined conditions. On September 4, 2013, upon satisfying one of the conditions, the Company issued the Convertible Notes with total aggregate proceeds of \$4.3 million. All of the Convertible Notes were purchased by current Preferred Stockholders. The Convertible Notes accrue interest at 8% per annum and mature on or after March 31, 2014 upon written notice from a majority of the outstanding Convertible Note holders (the "Maturity Date").

In connection with the issuance of the Convertible Notes, the Company incurred \$36,000 of financing costs which were recorded in other current assets. The Company also reimbursed the lenders \$10,000 for financing costs which has been recorded as a discount on the Convertible Notes. The Convertible Notes included various embedded conversion and redemption features as further described below. The Company recorded approximately \$1.4 million as the fair value of the combined embedded derivative liability on September 4, 2013, with a corresponding amount recorded as debt discount. The debt discount has been amortized to interest expense over the life of the Convertible Notes. As of December 31, 2013 and March 31, 2014 (unaudited), the fair value of the combined embedded derivative liability was \$1.4 million and \$1.5 million, respectively. Amounts recorded for issuance costs and embedded features are being amortized to interest expense over the life of the Convertible Notes, approximately seven months. Changes in the estimated fair value of the embedded features are recorded in earnings in the period in which they occur.

The Convertible Notes provide for conversion upon maturity at the holder's option and mandatory conversion upon a reverse acquisition. Both of these features provide for the conversion of the outstanding principal of the Convertible Notes, plus accrued interest into Series C Preferred Stock at \$1.15 per share.

In the event the Company issues or sells equity securities prior to the Maturity Date with aggregate proceeds of not less than \$7.0 million, the Convertible Notes plus all accrued interest automatically convert into either (i) the newly issued equity securities at 75% of the cash price per share paid by the investors in the new equity securities; or (ii) shares of Series C Preferred Stock at \$1.15 per share. In accordance with ASC 815, the Company determined that this embedded mandatory conversion feature should be separately accounted for as a freestanding financial instrument as the conversion feature was a substantial contingent call option.

In the event the Company issues or sells equity securities prior to the Maturity Date with aggregate proceeds less than \$7.0 million, the Convertible Notes plus all accrued interest can be converted at the option of the holders into the newly issued equity securities at 75% of the cash price per share paid by the investors in the new equity securities. In accordance with ASC 815, the Company determined that this embedded conversion feature should be separately accounted for as a freestanding financial instrument as the conversion feature was a substantial contingent call option.

Notes to Financial Statements (Continued)

5. Convertible Notes (Continued)

In the event of a change in control of the Company prior to the Maturity Date, the Company has the option to prepay the Convertible Notes at 1.5 times principal, plus accrued interest. In accordance with ASC 815, the Company determined that this embedded redemption feature should be separately accounted for as a free-standing financial instrument as the conversion feature was a substantial contingent call option.

The Convertible Notes include a call feature, at the issuer's option, whereby the Convertible Notes may be prepaid at 1.5 times principal, plus accrued interest. In accordance with ASC 815, the Company determined that this embedded redemption feature should be separately accounted for as a free-standing financial instrument.

The Convertible Notes include a put feature, at the option of the holders, whereby upon a breach of the Note Agreement, repayment of the Convertible Notes can be accelerated at 1.5 times principal, plus accrued interest. In accordance with ASC 815, the Company determined that this embedded redemption feature should be separately accounted for as a free-standing financial instrument. The Convertible Notes also include an additional put feature, at the option of the holders, whereby upon an event of default, the repayment of the Convertible Notes can be accelerated in the amount of the outstanding principal, plus accrued interest. In accordance with ASC 815, the Company determined that this embedded redemption feature does not require separate accounting as a free-standing financial instrument.

The embedded features requiring separate accounting were combined and valued upon issuance using a single income valuation approach. The Company estimated the fair value of the combined embedded derivative identified above using a "with and without" income valuation approach. Under this approach, the Company estimated the present value of the fixed interest rate debt based on the fair value of similar debt instruments excluding the embedded features. This amount was then compared to the fair value of the debt instrument including the embedded features using a probability weighted approach by assigning each embedded derivative feature a probability of occurrence, with consideration provided for the settlement amount including conversion discounts, prepayment penalties, the expected life of the liability and the applicable discount rate.

As of September 4, 2013, December 31, 2013, and March 31, 2014 (unaudited), the Company ascribed a probability to the mandatory conversion feature upon a financing of not less than \$7.0 million of 85%, 100% and 100%, respectively. As of September 4, 2013, December 31, 2013, and March 31, 2014 (unaudited) the Company ascribed a probability to the call feature upon a change in control of 15%, 0% and 0%, respectively. For all other features included in the combined embedded derivative, the Company estimated a 0% probability of occurrence as of September 4, 2013, December 31, 2013 and March 31, 2014 (unaudited). The Company classified the liability within Level 3 of the fair value hierarchy as the probability factor is an unobservable input and significant to the valuation model.

## Notes to Financial Statements (Continued)

## 6. Accrued expenses

Accrued expenses consist of the following (in thousands):

	December 31,		March 31,
	2012	2013	2014 (unaudited)
Payroll and employee-related costs	\$ 81	\$ 419	\$ 553
Contracted service costs	544	360	736
Professional fees	95	202	332
Other	15	3	3
<b>Total</b>	<b>\$ 735</b>	<b>\$ 984</b>	<b>\$ 1,624</b>

## 7. Option to Acquire Company

In March 2009, the Company entered into an option agreement with a major pharmaceutical entity that provides an exclusive option to acquire the Company under a pre-negotiated merger agreement. The Company received a \$10.0 million non-refundable payment as consideration for the agreement. The fair value of the option to acquire the Company was estimated using the Black-Scholes option-pricing model with the following assumptions:

Expected volatility	76%
Expected option expiration date	June 30, 2013
Expected dividends	0%
Expected term (years)	4.34
Risk-free rate	1.80%

Expected volatility was based on historical volatility of companies within the biotechnology industry. The exercise price of the option to acquire all outstanding shares of Company stock, prior to the payment of contingent program milestones, was \$240.0 million. The fair value of the option to acquire all of the outstanding shares of the Company was estimated to be \$7.1 million, which was recorded as additional paid-in capital during 2009. The \$2.9 million difference between the \$10.0 million non-refundable payment and the fair value of the option was recorded as deferred revenue during 2009, representing the value of certain residual rights in the event the acquisition option is not exercised (e.g., a right, under certain circumstances, to license the Company's underlying technology). The acquisition option expired unexercised in 2013. This amount will not be recognized as revenue until the residual rights lapse, which will occur during the second half of 2014.

## 8. Commitments and Contingencies

## Significant Contracts and Agreements

In February 2002, the Company entered into an agreement to license certain intellectual property from Johns Hopkins University. The agreement calls for payments to be made by the Company upon the commencement of product sales, in the form of a royalty of 2.5% on net sales of the product. As the Company has not commenced product sales, during the years ended December 31, 2012 and 2013 and the three months ended March 31, 2014 (unaudited), the Company has recognized no royalties on product sales.

Notes to Financial Statements (Continued)

8. Commitments and Contingencies (Continued)

Operating Leases

The Company has various non-cancellable operating leases for facilities and office equipment that expire at various dates through 2014. The facility leases require the Company to pay all electricity costs. Rental expense for the years ended December 31, 2012 and 2013, and three months ended March 31, 2013 and 2014 (unaudited) was \$0.3 million, \$0.2 million, \$47,000 and \$47,000, respectively.

Future annual minimum lease payments through 2014 from the period ending March 31, 2014 are \$0.1 million (unaudited).

*Restricted cash related to facilities leases*

At December 31, 2012 and 2013, and March 31, 2014 (unaudited), the Company had \$38,000 in an outstanding letter of credit to be used as collateral for leased premises. At December 31, 2012 and 2013 and March 31, 2014 (unaudited), the Company has pledged an aggregate of \$39,000 to the bank as collateral for the letter of credit, which is included in short-term deposits.

9. Redeemable Convertible Preferred Stock

As of December 31, 2013 and March 31, 2014 (unaudited), the total authorized capital stock of the Company was 172,222,978 shares, which included 22,638,465 shares of Series A Preferred Stock, \$0.001 par value per share; 10,909,091 shares of Series A-1 Preferred Stock, \$0.001 par value per share; 20,754,461 shares of Series B Preferred Stock, \$0.001 par value per share; and 17,550,758 shares of Series C Preferred Stock, \$0.001 par value per share.

Conversion

Shares of Series C Preferred Stock, Series B Preferred Stock, Series A-1 Preferred Stock and Series A Preferred Stock are convertible into Common stock initially on a one-for-one basis adjustable for certain dilutive events. All outstanding shares of Preferred Stock are automatically convertible based on either: (i) stockholder approval, as defined in the Certificate of Incorporation, or (ii) the closing of a firm-commitment, underwritten IPO, in which the aggregate proceeds are at least \$40 million with an offering price of at least \$3.45 per share of Common Stock. The Preferred Stock conversion price is subject to adjustment in the event additional shares of Common Stock or certain securities convertible into Common Stock, are issued for consideration per share less than the respective Preferred Stock conversion price.

Dividends

Holders of Preferred Stock are entitled to two types of dividends:

*Accruing Dividends*

Holders of the Series C Preferred Stock, Series B Preferred Stock, Series A-1 Preferred Stock and Series A Preferred Stock are entitled to receive, when and if declared by the Board of Directors, dividends at the annual rate of \$0.0805, \$0.0805, \$0.077 and \$0.07 per share, subject to adjustment for stock dividends, stock splits, combinations, recapitalizations, or the like, with respect to such shares. The Preferred Stock Accruing Dividends are cumulative and non-compounding. An aggregate of \$22.5 million,

Notes to Financial Statements (Continued)

**9. Redeemable Convertible Preferred Stock (Continued)**

\$27.6 million, and \$28.9 million of accruing dividends have been recorded for the Preferred Stock as of December 31, 2012 and 2013, and March 31, 2014 (unaudited), respectively.

***Non-Cumulative Dividends***

Holders of the Series C Preferred Stock, Series B Preferred Stock, Series A-1 Preferred Stock and Series A Preferred Stock are entitled to receive, when and if declared by the Board of Directors, dividends at the annual rate of 7% of the issue price per share, subject to adjustment for stock dividends, stock splits, combinations, recapitalizations, or the like, with respect to such shares. These dividends are non-cumulative and non-compounding.

The Company shall not declare, pay, or set aside any dividends on Common stock (other than those payable in shares of Common stock) unless the holders of the Preferred Stock then outstanding shall first receive, or simultaneously receive, a dividend on each outstanding share of Preferred Stock in an amount at least equal to or greater than the product of (i) the dividend payable on each share of Common stock and (ii) the number of shares of Common stock issuable upon conversion of a share of Preferred Stock calculated on the record date for determination of holders entitled to receive such a dividend.

***Liquidation Preference***

Holders of the Series C Preferred Stock have preference in the event of a liquidation or dissolution of the Company equal to \$1.15 per share, plus any declared dividends, but specifically excluding any Accruing Dividends. Holders of the Series B Preferred Stock have preference in the event of a liquidation or dissolution of the Company, which preference is junior to the liquidation preference for the Series C Preferred Stock, equal to \$1.15 per share, plus any declared dividends, but specifically excluding any Accruing Dividends. Holders of the Series A Preferred Stock and the Series A-1 Preferred Stock have preference in the event of a liquidation or dissolution of the Company, which preference is junior to the liquidation preference for the Series C Preferred Stock and the Series B Preferred Stock, equal to \$1.00 per share and \$1.10 per share, plus any declared dividends, respectively but specifically excluding any Accruing Dividends

After all preferred stockholders have received their respective initial preference amounts, any assets remaining for distribution shall be distributed to the holders of the Series C Preferred Stock, Series B Preferred Stock, Series A-1 Preferred Stock, Series A Preferred Stock and Common Stock pro rata in proportion to the total number of shares of Series C Preferred Stock, Series B Preferred Stock, Series A-1 Preferred Stock, Series A Preferred Stock and Common Stock, assuming conversion to Common Stock. As of March 31, 2014 (unaudited), the aggregate liquidation value for the Series C Preferred Stock, Series B Preferred Stock, Series A-1 Preferred Stock and Series A Preferred Stock was \$22.6 million, \$12.0 million, \$23.9 million and \$15.2 million, respectively. Refer to Note 15 for further details.

***Voting Rights***

Except for matters with specific voting rights, the holders of shares of Preferred Stock vote together with the holders of the Common Stock as a single class on any matter presented to the stockholders of the Company for their action or consideration at any meeting of the stockholders of the Company or by written consent of stockholders in lieu of meetings. The holders of the Preferred Stock are entitled to the number of votes equal to the number of shares of Common Stock into which each share of the Preferred Stock is convertible at the time of such vote. A vote of 70% of the Preferred Stockholders, voting as a

Notes to Financial Statements (Continued)

**9. Redeemable Convertible Preferred Stock (Continued)**

single class, is required for events that would materially affect the business or change the rights of the Preferred Stock. A vote of the majority of the Series B Preferred Stockholders that do not also hold Series C Preferred Stock, Series A-1 Preferred Stock or Series A Preferred Stock, voting as a single class, is required for certain actions that affect the designations, powers, preference, rights, restrictions or number of shares of Series B Preferred Stock. The holders of Series A-1 Preferred Stock and Series A Preferred Stock, exclusively and as a separate class, have the right to elect three of the seven Directors. The holders of Series B Preferred Stock, exclusively and as a separate class, have the right to elect one of the seven Directors.

**Redemption Rights**

Each class of Preferred Stock is stated at its then current redemption value as of each balance sheet date presented.

The Preferred Stock may be redeemed upon written election of the holders of 70% of the Series C Preferred Stock, Series B Preferred Stock, Series A-1 Preferred Stock and Series A Preferred Stock on or after August 2, 2016. The Series C Preferred Stock, Series B Preferred Stock, Series A-1 Preferred Stock and Series A Preferred Stock will receive, through a series of three installments, \$1.15, \$1.15, \$1.10 and \$1.00, respectively, per share (subject to certain adjustments) plus any Accruing Dividends accrued but unpaid thereon, whether or not declared, together with any other dividends declared but unpaid thereon.

If the Company does not have sufficient funds available to redeem all shares of Preferred Stock, then the Company shall redeem first, a pro rata portion of each holder's Series C Preferred Stock to the fullest extent of the funds available and shall redeem the remaining shares of Series C Preferred Stock as funds become available until all shares of Series C Preferred Stock have been redeemed in full. Then, it shall redeem a pro rata portion of each holder's Series B Preferred Stock to the fullest extent of the funds available and shall redeem the remaining shares of Series B Preferred Stock as soon as practicable as funds become available until all shares of Series B Preferred Stock have been redeemed in full. Then, it shall redeem a pro rata portion of each holder's Series A Preferred Stock and Series A-1 Preferred Stock out of funds available and shall redeem the remaining shares of Series A Preferred Stock and Series A-1 Preferred Stock as soon as funds become available for such purpose. Refer to Note 15 for further details.

**10. Common Stock**

**General**

The voting, dividend and liquidation rights of the holders of shares of Common Stock are subject to and qualified by the rights, powers and preferences of the holders of shares of Preferred Stock. The Common Stock has the following characteristics:

**Voting**

The holders of shares of Common stock are entitled to one vote for each share of Common Stock held at all meetings of stockholders and written action in lieu of meetings; there is no cumulative voting.

**Dividends**

The holders of shares of Common Stock are entitled to receive dividends, if and when declared by the Board of Directors. Cash dividends may not be declared or paid to holders of shares of Common Stock until paid on each series of outstanding Preferred Stock in accordance with their respective terms. As of March 31, 2014 (unaudited), no dividends have been declared or paid since the Company's inception.

## Notes to Financial Statements (Continued)

## 10. Common Stock (Continued)

*Liquidation*

After payment to the holders of shares of Preferred Stock of their liquidation preferences, the holders of the Common Stock are entitled to share ratably in the Company's assets available for distribution to stockholders, in the event of any voluntary or involuntary liquidation, dissolution or winding up of the Company or upon the occurrence of a deemed liquidation event.

*Reserve for future issuance*

The Company has reserved for future issuances the following number of shares of Common Stock:

	December 31,		March 31,
	2012	2013	2014
Conversion of Series A Preferred Stock	22,638,465	22,638,465	22,638,465
Conversion of Series A-1 Preferred Stock	10,909,091	10,909,091	10,909,091
Conversion of Series B Preferred Stock	20,754,461	20,754,461	20,754,461
Conversion of Series C Preferred Stock	17,550,758	17,550,758	17,550,758
Stock-based compensation awards	10,036,341	9,888,775	9,885,025
Warrants to purchase Common Stock	10,471,282	10,471,282	10,471,282
<b>Total</b>	<b>92,360,398</b>	<b>92,212,832</b>	<b>92,209,082</b>

The above table does not include the 52,813,827 shares of Common Stock that relate to the shares of Series D convertible Preferred Stock that were issued on May 13, 2014 and that convert on a 1-for-1 basis into shares of Common Stock. Please refer to Note 15 for more detail.

## 11. Stock-based Compensation

In March 2006, the Company adopted the 2006 Equity Incentive Plan (the "Plan"). Under the Plan, the Company has granted stock options to selected officers, employees and consultants of the Company. As of March 31, 2014 (unaudited), the Plan, as amended, provides for the issuance of up to 10,084,201 shares of Common Stock. As a result of the May 2014 Series D financing this number was modified (see Note 15).

Terms of stock award agreements, including vesting requirements, are determined by the Board of Directors, subject to the provisions of the Plan. Option and share awards generally vest over three to four years. Certain option and share awards provide for accelerated vesting if there is a change in control as defined in the Plan. The options are exercisable from the date of grant for a period of ten years. For options granted to date, the exercise price equaled the fair value of the Common Stock as determined by the Board of Directors on the date of grant.

Stock options issued to non-employees are accounted for using the fair value method of accounting, are periodically revalued as the options vest and are recognized as expense over the related service period. The total expense related to all options granted to non-employees for the years ended December 31, 2012 and 2013, the three months ended March 31, 2013 and 2014 (unaudited) was \$9,000, \$32,000, \$10,000 and \$2,000, respectively.

Notes to Financial Statements (Continued)

11. Stock-based Compensation (Continued)

Total stock-based compensation expense is recognized for stock options granted to employees and non-employees and has been reported in the Company's statements of operations as follows (in thousands):

	Years Ended December 31,		Three Months Ended March 31,	
	2012	2013	2013 (unaudited)	2014 (unaudited)
Research and development	\$ 46	\$ 106	\$ 70	\$ 10
General and administrative	64	49	13	7
Total	<u>\$ 110</u>	<u>\$ 155</u>	<u>\$ 83</u>	<u>\$ 17</u>

A following table summarizes stock option activity for employees and non-employees (intrinsic value in thousands):

	Shares	Weighted- Average Exercise Price	Weighted- Average Remaining Contractual Term (years)	Aggregate Intrinsic Value
Outstanding at December 31, 2012	9,737,684	\$ 0.13	6.2	\$ 12,370
Granted	50,000	\$ 1.40		
Exercised	(147,566)	\$ 0.13		
Cancelled or forfeited	(6,748)	\$ 0.16		
Outstanding at December 31, 2013	<u>9,633,370</u>	\$ 0.14	5.2	\$ 1,627
Granted (unaudited)	—	\$ —		
Exercised (unaudited)	(3,750)	\$ 0.08		
Cancelled or forfeited (unaudited)	—	\$ —		
Outstanding at March 31, 2014 (unaudited)	<u>9,629,620</u>	\$ 0.14	5.0	\$ 1,627
Exercisable at December 31, 2013	<u>8,087,507</u>	\$ 0.14	4.7	\$ 1,307
Vested or expected to vest at December 31, 2013(1)	<u>9,262,144</u>	\$ 0.14	5.1	\$ 1,561
Exercisable at March 31, 2014 (unaudited)	<u>8,303,728</u>	\$ 0.14	4.9	\$ 1,593
Vested or expected to vest at March 31, 2014 (unaudited)(1)	<u>9,293,580</u>	\$ 0.14	4.9	\$ 1,568

- (1) This represents the number of vested options at December 31, 2013 and March 31, 2014 (unaudited), plus the number of unvested options expected to vest at December 31, 2013 and March 31, 2014 (unaudited), based on the unvested options outstanding at December 31, 2013 and March 31, 2014 (unaudited).

During the year ended December 31, 2012, the Company did not grant stock options. During the year ended December 31, 2013 and the three months ended March 31, 2013 (unaudited), the Company granted stock options to purchase an aggregate of 50,000 shares of its Common Stock with a weighted-average



Notes to Financial Statements (Continued)

**11. Stock-based Compensation (Continued)**

grant date fair value of \$1.04. The Company did not grant stock options in the three months ended March 31, 2014 (unaudited).

The total intrinsic value of options exercised in the years ended December 31, 2012 and 2013 and three months ended March 31, 2013 and 2014 (unaudited), was \$0, \$0.1 million, \$0 and \$1,000, respectively. As of March 31, 2014 (unaudited), there was \$0.1 million of total unrecognized compensation cost related to employee non-vested stock options granted under the Plan. As of March 31, 2014 (unaudited), the unrecognized compensation cost related to non-employee, non-vested stock options granted under the plan was \$4,000.

The total unrecognized compensation cost for employee and non-employee awards will be adjusted for future forfeitures. The Company expects to recognize that cost over a remaining weighted-average period of two years.

During 2013, the Company modified the stock option awards of one employee upon the employee's termination. In accordance with ASC 718, the Company assessed the fair value of the unvested portion of the modified awards at \$0.1 million, and recorded the amount as compensation cost on the date of termination.

The Company estimates the fair value of each employee stock award on the grant date using the Black-Scholes option-pricing model based on the following assumptions regarding the fair value of the underlying Common Stock on each measurement date:

	Year Ended December 31, 2013
Weighted average expected volatility	91.12%
Expected term (in years)	5.95
Risk free interest rate	1.03%
Expected dividend yield	0%

**12. 401(k) Savings Plan**

In October 2007, the Company adopted a tax-qualified employee savings and retirement 401(k) Plan, covering all qualified employees. Participants may elect a salary deferral of at least 1% as a contribution to the 401(k) Plan, up to the statutorily prescribed annual limit for tax-deferred contributions. The Company may elect to make a safe harbor contribution to the Plan equal to 3% of each eligible employee's salary. Safe harbor contributions are fully vested to plan participants at all times. The Company had no safe harbor contributions for the years ended 2012 and 2013 and the three months ended March 31, 2014 (unaudited).

**13. Income Taxes**

For the years ended December 31, 2012 and 2013, the three months ended March 31, 2013 and 2014 (unaudited) the Company has not recorded a provision for federal or state income taxes as it has had cumulative net operation losses since inception. The Company's losses before income taxes consist solely of domestic losses.

Notes to Financial Statements (Continued)

13. Income Taxes (Continued)

A reconciliation of income taxes computed using the U.S. federal statutory rate to that reflected in operations follows (in thousands):

	Years Ended December 31,	
	2012	2013
Income tax benefit using U.S. federal statutory rate	\$ (2,710)	\$ (2,690)
Permanent differences	38	299
State income taxes, net of federal benefit	(368)	(389)
Tax credits	(95)	(7,164)
Expiring net operating losses and tax credits	287	2,566
Change in the valuation allowance	2,988	7,286
Other	(140)	92
	<u>\$ —</u>	<u>\$ —</u>

The significant components of the Company's deferred tax assets are as follows (in thousands):

	Years Ended December 31,	
	2012	2013
Net operating loss carryforwards	\$ 26,560	\$ 26,304
Federal and state tax credits	2,777	9,941
Deferred revenue	1,139	1,147
Accrued expenses	155	332
Patents	692	612
Other	27	300
	<u>31,350</u>	<u>38,636</u>
Valuation allowance	<u>(31,350)</u>	<u>(38,636)</u>
Net deferred tax asset	<u>\$ —</u>	<u>\$ —</u>

Management of the Company has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets. Based on the Company's history of operating losses, management of the Company has concluded that it is more likely than not that the benefit of its deferred tax assets will not be realized. Accordingly, the Company has provided a full valuation allowance for deferred tax assets as of December 31, 2012 and 2013.

The valuation allowance increased approximately \$7.3 million during the year ended December 31, 2013, due primarily to the addition of Orphan Drug Tax credits for 2009 through 2012 as well as the generation of net operating losses during the year ended December 31, 2013, both of which are fully reserved. The valuation allowance increased approximately \$3.0 million during the year ended December 31, 2012, due primarily to the generation of net operating losses during the period.

Subject to the limitations described below, as of December 31, 2012 and 2013, the Company has net operating loss carryforwards of approximately \$70.3 million and \$69.9 million, respectively, to offset future federal taxable income, which will expire at various times between 2026 and 2033. The Company does not have any net operating losses that are attributable to excess stock option deductions which would be

Notes to Financial Statements (Continued)

**13. Income Taxes (Continued)**

recorded as an increase in additional paid-in capital. As of December 31, 2012 and 2013, the Company has state net operating loss carryforwards of approximately \$50.4 million and \$45.4 million, respectively, to offset future state taxable income, which will expire at various times between 2014 and 2033. As of December 31, 2012 and 2013, the Company has tax credit carryforwards of approximately \$3.1 million and \$10.3 million, respectively, to offset future federal and state income taxes, which will expire at various times between 2022 and 2033.

Net operating loss and tax credit carryforwards are subject to review and possible adjustment by the Internal Revenue Service (the "IRS") and may become subject to an annual limitation in the event of certain cumulative changes in the ownership interest of significant shareholders over a three-year period in excess of 50% as defined under Sections 382 and 383 in the Internal Revenue Code. This could substantially limit the amount of tax attributes that can be utilized annually to offset future taxable income or tax liabilities. The amount of the annual limitation is determined based on the Company's value immediately prior to the ownership change. Subsequent ownership changes may further affect the limitation in future years.

The Company had no unrecognized tax benefits or related interest and penalties accrued during the years ended December 31, 2012 and 2013. The Company will recognize interest and penalties related to uncertain tax positions in income tax expense.

The Company is subject to U.S. federal income tax and primarily Massachusetts state income tax. The statute of limitations for assessment by the IRS and state tax authorities is open for tax years ending December 31, 2010 through 2013, although carryforward attributes that were generated prior to tax year 2010 may still be adjusted upon examination by the IRS or state tax authorities if they either have been or will be used in a future period. Currently, no federal or state income tax returns are under examination by the respective taxing authorities.

**14. Net loss Per Share Attributable to Common Stockholders**

As described in Note 2, *Summary of Significant Accounting Policies*, the Company computes basic and diluted earnings (loss) per share using a methodology that gives effect to the impact of outstanding participating securities (the "two-class method"). As the years ended December 31, 2012 and 2013, and the three months ended March 31, 2013 and 2014 (unaudited) resulted in net losses, there is no income allocation required under the two-class method or dilution attributed to weighted average shares outstanding in the calculation of diluted loss per share.

## Notes to Financial Statements (Continued)

## 14. Net loss Per Share Attributable to Common Stockholders (Continued)

The following Common Stock equivalents, presented on an as converted basis, were excluded from the calculation of net loss per share for the periods presented, due to their anti-dilutive effect (in thousands):

	December 31,		March 31,	
	2012	2013	2013	2014
			(unaudited)	
Convertible preferred stock	67,505	67,505	67,505	67,505
Common stock warrants	10,471	10,471	10,471	10,471
Outstanding stock options	9,738	9,633	9,788	9,629
Convertible notes	—	3,870	—	3,945
	<u>87,714</u>	<u>91,479</u>	<u>87,764</u>	<u>91,550</u>

## 15. Subsequent Events (unaudited)

On May 13, 2014, the Company issued 52,813,827 shares of Series D convertible Preferred Stock to new and existing investors at a price of \$0.588656 per share for gross proceeds of \$25.0 million. This included the issuance of 10,344,201 shares of Series D convertible Preferred Stock as a result of converting \$4.5 million of Convertible Notes and accrued interest that were issued in September 2013 at a conversion price of \$0.4414. The redemption date for all other series of Redeemable Convertible Preferred Stock was extended to May 2019 as a result of this issuance.

Upon liquidation, the holders of shares of each series of Preferred Stock are entitled to be paid out of the assets of the Company available for distribution to its stockholders, on a pari passu basis, before any payment shall be made to the holders of Common Stock. The holders of the Series D Preferred Stock are entitled to receive an amount equal to \$0.588656 per share plus declared but unpaid dividends. After the payment of all preferential amounts required to be paid upon liquidation to the holders of the Series D Preferred Stock, the holders of the Series C Preferred Stock are entitled to receive an amount equal to \$0.6242 per share plus declared but unpaid dividends. After the payment of all preferential amounts required to be paid upon liquidation to the holders of the Series C Preferred Stock, the holders of the Series B Preferred Stock are entitled to receive an amount equal to \$0.6242 per share plus declared but unpaid dividends. After the payment of all preferential amounts required to be paid upon liquidation to the holders of the Series B Preferred Stock, the holders of the Series A Preferred Stock and the holders of the Series A-1 Preferred Stock are entitled to receive an amount equal to \$0.5428 and \$0.5971 per share, respectively, plus declared but unpaid dividends. All other rights of the Series D Preferred Stock are consistent with the rights of the Series A, Series A-1, Series B and Series D Preferred Stock.

Per the Restated Certificate of Incorporation filed in connection with the issuance of the Series D Preferred Stock, the Series A Preferred Stock, Series A-1 Preferred Stock, Series B Preferred Stock and Series C Preferred Stock conversion prices were modified as follows: the Series A Preferred Stock converts into the number of shares of Common Stock as determined by dividing the applicable purchase price by the applicable conversion price of \$0.8388; the Series A-1 Preferred Stock converts into the number of shares of Common Stock as determined by dividing the applicable purchase price by the applicable conversion price of \$0.9022; the Series B Preferred Stock converts into the number of shares of Common Stock as determined by dividing the applicable purchase price by the applicable conversion price of

Notes to Financial Statements (Continued)

**15. Subsequent Events (unaudited) (Continued)**

\$0.9339; and the Series C Preferred Stock converts into the number of shares of Common Stock as determined by dividing the applicable purchase price by the applicable conversion price of \$0.9339.

In connection with the issuance of the Series D Preferred Stock, the Company filed a Restated Certificate of Incorporation pursuant to Sections 242 and 245 of the General Corporation Law of the State of Delaware on May 9, 2014. As part of the Restated Certificate of Incorporation, the Company increased its authorized shares of Common Stock to 205,926,290 shares and increased the shares available under the 2006 Stock Incentive Plan by 8,137,956 shares.

On June 24, 2014 the Board of Directors approved a grant of 8,375,000 stock options at an exercise price of \$0.31 per share to our employees and certain non-employee Directors. On the first anniversary of the vesting commencement date, 25% of the options will vest, and the remainder vest in 12 equal quarterly installments over the following three years. The options have a life of 10 years.

**Shares**

**Common Stock**



**, 2014**

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**Stifel**

**JMP Securities**

**Baird**

**Oppenheimer & Co.**

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Until \_\_\_\_\_, 2014 (25 days after the date of this prospectus), all dealers that effect buy, sell or trade shares of our common stock, whether or not participating in this offering, may be required to deliver a prospectus. This is in addition to the dealers' obligation to deliver a prospectus when acting as underwriter and with respect to their unsold allotments or subscriptions.

Neither we nor any of the underwriters have authorized anyone to provide information different from that contained in this prospectus. When you make a decision about whether to invest in our common stock, you should not rely upon any information other than the information in this prospectus. Neither the delivery of this prospectus nor the sale of our common stock means that information contained in this prospectus is correct after the date of this prospectus. This prospectus is not an offer to sell or solicitation of an offer to buy these shares of common stock in any circumstances under which the offer or solicitation is unlawful.

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**PART II****INFORMATION NOT REQUIRED IN PROSPECTUS****Item 13. Other Expenses of Issuance and Distribution.**

The following table sets forth the fees and expenses in connection with the issuance and distribution of the securities being registered (excluding the underwriting discount). Except for the Securities and Exchange Commission registration fee and the FINRA filing fee, all amounts are estimates.

	<u>Amount Paid or to be Paid</u>
SEC registration fee	\$ *
FINRA filing fee	*
NASDAQ listing fee	*
Legal fees and expenses	*
Accounting fees and expenses	*
Printing expenses	*
Transfer agent fees and expenses	*
Miscellaneous	*
Total	<u>\$ *</u>

\* To be filed by amendment.

**Item 14. Indemnification of Directors and Officers.**

Section 145 of the Delaware General Corporation Law authorizes a corporation's board of directors to grant, and authorizes a court to award, indemnity to officers, directors, and other corporate agents.

As permitted by Delaware law, our certificate of incorporation, which will be amended and restated and in effect upon the completion of the offering, provides that, to the fullest extent permitted by Delaware law, no director will be personally liable to us or our stockholders for monetary damages for breach of fiduciary duty as a director. Pursuant to Delaware law such protection would be not available for liability:

- for any breach of a duty of loyalty to us or our stockholders;
- for acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law;
- for any transaction from which the director derived an improper benefit; or
- for an act or omission for which the liability of a director is expressly provided by an applicable statute, including unlawful payments of dividends or unlawful stock repurchases or redemptions as provided in Section 174 of the Delaware General Corporation Law.

Our amended and restated certificate of incorporation also provides that if Delaware law is amended after the approval by our stockholders of the amended and restated certificate of incorporation to authorize corporate action further eliminating or limiting the personal liability of directors, then the liability of our directors will be eliminated or limited to the fullest extent permitted by Delaware law.

Our bylaws, which will be amended and restated and in effect upon the completion of the offering, further provide that we must indemnify our directors and officers to the fullest extent permitted by Delaware law. The amended and restated bylaws also authorize us to indemnify any of our employees or agents and permit us to secure insurance on behalf of any officer, director, employee or agent for any liability arising out of his or her action in that capacity, whether or not Delaware law would otherwise permit indemnification.

In addition, our amended and restated bylaws provide that we are required to advance expenses to our directors and officers as incurred in connection with legal proceedings against them for which they may be indemnified and that the rights conferred in the amended and restated bylaws are not exclusive.

At present, there is no pending litigation or proceeding involving any of our directors, officers or employees for which indemnification is sought, and we are not aware of any threatened litigation that may result in claims for indemnification.

We intend to enter into indemnification agreements with each of our directors and executive officers. These agreements, among other things, would require us to indemnify each director and officer to the fullest extent permitted by Delaware law, the amended and restated certificate of incorporation and amended and restated bylaws, for expenses such as, among other things, attorneys' fees, judgments, fines, and settlement amounts incurred by the director or executive officer in any action or proceeding, including any action by or in our right, arising out of the person's services as our director or executive officer or as the director or executive officer of any subsidiary of ours or any other company or enterprise to which the person provides services at our request. We also maintain directors' and officers' liability insurance.

The SEC has taken the position that personal liability of directors for violation of the federal securities laws cannot be limited and that indemnification by us for any such violation is unenforceable. The limitation of liability and indemnification provisions in our amended and restated certificate of incorporation and amended and restated bylaws may discourage stockholders from bringing a lawsuit against our directors and officers for breach of their fiduciary duty. They may also reduce the likelihood of derivative litigation against our directors and officers, even though an action, if successful, might benefit us and other stockholders. Further, a stockholder's investment may be adversely affected to the extent that we pay the costs of settlement and damage awards against directors and officers as required by these indemnification provisions.

## **Item 15. Recent Sales of Unregistered Securities**

Set forth below is information regarding securities we have issued within the past three years that were not registered under the Securities Act:

### **(1) Issuances of Capital Stock**

On August 2, 2011, the Registrant issued and sold to investors an aggregate of 13,202,932 shares of its Series C preferred stock and warrants to purchase 10,471,282 shares of its common stock, at a purchase price of \$1.15 per share, for aggregate consideration of approximately \$15,183,371, which was paid for in cash.

On May 13, 2014, the Registrant issued and sold to investors an aggregate of 52,813,827 shares of its Series D preferred stock, at a purchase price of \$0.588656 per share, for aggregate consideration of \$25,000,000. This included 10,344,201 shares of its Series D preferred stock in exchange for conversion of approximately \$4,565,934 of principal indebtedness and unpaid accrued interest thereon under the promissory notes described in paragraph (2) below, at a conversion price of \$0.4414 per share, which represented a 25% discount on the purchase price per share of the Registrant's Series D preferred stock issued and sold in the offering.

### **(2) Sale of Convertible Promissory Notes**

On September 4, 2013, the Registrant issued and sold to investors convertible promissory notes in the aggregate principal amount of \$4,338,660, which notes bore interest at the rate of 8% per annum.

### **(3) Stock Option Grants and Exercises**

During the three-year period ended June 24, 2014, we have granted to employees, consultants and directors options to purchase 11,804,569 shares of our common stock under our 2006 Equity Incentive



Plan, as amended and in effect from time to time. The exercise price per share ranged from \$0.08 to \$1.40. Options to purchase shares of our common stock pursuant to our 2006 Equity Incentive Plan, as amended and in effect from time to time, generally vest either 25% on the first anniversary of the vesting start date, with the remainder vesting in 12 equal quarterly installments, or in 16 equal quarterly installments.

During the three year period ended June 24, 2014, an aggregate of 221,676 shares of our common stock were issued upon exercise of outstanding stock options granted under our 2006 Equity Incentive Plan, as amended and in effect from time to time, with exercise prices ranging from \$0.08 to \$0.20 per share.

No underwriters were involved in the foregoing issuances of securities. The offers, sales and issuances of the securities described above were deemed to be exempt from registration under the Securities Act in reliance upon Rule 701 or Section 4(a)(2) of the Securities Act. The offers, sales and issuances of the securities that were deemed to be exempt in reliance on Rule 701 were transactions under compensatory benefit plans and contracts relating to compensation as provided under Rule 701. The offers, sales and issuances of the securities that were deemed to be exempt in reliance upon Section 4(a)(2) were each transactions not involving any public offering, and all recipients of these securities were accredited investors within the meaning of Rule 501 of Regulation D of the Securities Act who were acquiring the applicable securities for investment and not distribution and had represented that they could bear the risks of the investment. Each of the recipients of securities in these transactions had adequate access, through employment, business or other relationships, to information about us.

**Item 16. Exhibits and Financial Statement Schedules.**

**(a) Exhibits**

Exhibit No.	Description
1.1*	Form of Underwriting Agreement.
3.1	Fifth Amended and Restated Certificate of Incorporation of the Company, as currently in effect.
3.2*	Form of Amended and Restated Certificate of Incorporation of the Company, to be in effect upon completion of the offering.
3.3	Bylaws of the Company, as currently in effect.
3.4*	Form of Amended and Restated Bylaws of the Company, to be in effect upon completion of the offering.
4.1*	Form of Common Stock Certificate.
4.2*	Fourth Amended and Restated Investors' Rights Agreement, dated May 13, 2014, between the Company and certain investors named therein.
4.3*	Series D Preferred Stock Purchase Agreement, dated May 13, 2014, between the Company and certain investors named therein.
5.1*	Form of Opinion of Bingham McCutchen LLP.
10.1†	2006 Equity Incentive Plan, as amended on August 1, 2006, as further amended on June 25, 2007, as further amended on February 17, 2009, as further amended on February 25, 2009, as further amended on April 16, 2009, as further amended on August 2, 2011 and as further amended on May 8, 2014.
10.2*†	2014 Equity Incentive Plan.

<b>Exhibit No.</b>	<b>Description</b>
10.3*†	Employment Agreement by and between the Company and Timothy P. Noyes, dated April 14, 2006, as amended April 29, 2009.
10.4*†	Employment Agreement by and between the Company and Steven Burke, dated July 25, 2006, as amended April 29, 2009.
10.5†*	Employment Agreement by and between the Company and F. Nicholas Franano, dated March 29, 2006, as amended by that Modification and Separation Agreement dated October 31, 2009.
10.6*†	Employment Agreement by and between the Company and George Eldridge, dated September 9, 2013.
10.7‡	Process Development and Manufacturing Services Agreement by and between the Company and Lonza Ltd., dated September 1, 2009 (as amended by that Amendment No. 1 entered into as of February 21, 2012).
10.8*	Lease Agreement by and between the Company and Boston Properties Limited Partnership, dated July 13, 2009, as amended by that Amendment No. 1 dated September 14, 2012 as amended by that Amendment No. 2 dated October 17, 2013.
10.9	Assignment of Rights/License Agreement, effective as of February 4, 2002, by and between Johns Hopkins University and F. Nicholas Franano.
10.10	Assignment of Patent made and entered into as of December 30, 2002, by and between F. Nicholas Franano and Proteon Therapeutics, L.L.C.
10.11*	Letter agreement, dated October 1, 2010, among the National Institutes of Health, F. Nicholas Franano and the Company.
10.12*	Letter agreement, dated January 12, 2009, by and between F. Nicholas Franano and the Company (as successor-in-interest to Proteon Therapeutics, L.L.C.).
10.13*	Quitclaim Deed, dated January 17, 2011, by F. Nicholas Franano to the Company.
10.14‡	Form of Stock Option Grant Notice and Stock Option Agreement under the Company's 2006 Equity Incentive Plan, as amended.
10.15	Indemnification Agreement, dated as of March 29, 2006, by and between the Company and Brendan O'Leary.
10.16	Indemnification Agreement, dated as of June 26, 2007, by and between the Company and Hubert Birner.
10.17	Indemnification Agreement, dated as of September 12, 2012, by and between the Company and Todd Foley.
10.18*	Indemnification Agreement, dated as of February 6, 2013, by and between the Company and F. Nicholas Franano.
10.19	Indemnification Agreement, dated as of February 6, 2013, by and between the Company and Timothy P. Noyes.
10.20*	Indemnification Agreement, dated as of February 6, 2013, by and between the Company and Gregory D. Phelps.
10.21	Indemnification Agreement, dated as of May 13, 2014, by and between the Company and Tim Haines.

Exhibit No.	Description
10.22	Indemnification Agreement, dated as of May 13, 2014, by and between the Company and Dmitry Kobzyev.
21.1	List of Subsidiaries.
23.1*	Consent of Bingham McCutchen LLP (included in Exhibit 5.1).
23.2*	Consent of Ernst & Young LLP, independent registered public accounting firm.
24.1*	Power of Attorney (included on signature page).

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\* To be filed by amendment

† Indicates management contract or compensation plan

‡ Indicates confidential treatment has been requested with respect to specific portions of this exhibit. Omitted portions have been filed with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.

**(b) Financial Statement Schedules**

All schedules have been omitted because they are not required or because the required information is given in the financial statements or notes to those statements.

**Item 17. Undertakings.**

The undersigned Registrant hereby undertakes to provide to the underwriters at the closing specified in the underwriting agreement certificates in such denominations and registered in such names as required by the underwriters to permit prompt delivery to each purchaser.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the Registrant pursuant to the foregoing provisions, or otherwise, the Registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer or controlling person of the Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Act and will be governed by the final adjudication of such issue.

The undersigned Registrant hereby undertakes that:

- (1) For purposes of determining any liability under the Securities Act, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the Registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this registration statement as of the time it was declared effective.
- (2) For the purpose of determining any liability under the Securities Act, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.

**SIGNATURES**

Pursuant to the requirements of the Securities Act of 1933, as amended, the Registrant has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the city of Waltham, Commonwealth of Massachusetts on \_\_\_\_\_, 2014.

**PROTEON THERAPEUTICS, INC.**

By: \_\_\_\_\_

Timothy P. Noyes  
*President & Chief Executive Officer*

**POWER OF ATTORNEY**

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Timothy P. Noyes and George Eldridge his true and lawful attorney-in-fact and agent with full power of substitution, for him and in his name, place and stead, in any and all capacities, to sign any and all amendments (including post-effective amendments) to this registration statement, and to sign any registration statement for the same offering covered by the registration statement that is to be effective upon filing pursuant to Rule 462(b) promulgated under the Securities Act, and all post-effective amendments thereto, and to file the same, with all exhibits thereto and all documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorney-in-fact and agent, full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as he might or could do in person, hereby ratifying and confirming that all said attorneys-in-fact and agents or any of them, or his or their substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, as amended, this Registration Statement has been signed by the following persons in the capacities and on the dates indicated.

<u>Name</u>	<u>Title</u>	<u>Date</u>
Timothy P. Noyes	President, Chief Executive Officer and Director ( <i>Principal Executive Officer</i> )	_____, 2014
George Eldridge	Chief Financial Officer ( <i>Principal Financial Officer and Principal Accounting Officer</i> )	_____, 2014
Hubert Birner, Ph.D.	Director	_____, 2014
Todd Foley	Director	_____, 2014
F. Nicholas Franano, M.D.	Director	_____, 2014
John G. Freund, M.D.	Director	_____, 2014
Tim Haines	Director	_____, 2014
Dmitry Kobzyev, Ph.D.	Director	_____, 2014
Brendan M. O'Leary, Ph.D.	Director	_____, 2014
Gregory D. Phelps	Director	_____, 2014

**EXHIBIT INDEX**

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10.22	Indemnification Agreement, dated as of May 13, 2014, by and between the Company and Dmitry Kobzyev.
21.1	List of Subsidiaries.
23.1*	Consent of Bingham McCutchen LLP (included in Exhibit 5.1).
23.2*	Consent of Ernst & Young LLP, independent registered public accounting firm.
24.1*	Power of Attorney (included on signature page).

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\* To be filed by amendment

† Indicates management contract or compensation plan

‡ Indicates confidential treatment has been requested with respect to specific portions of this exhibit. Omitted portions have been filed with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.

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**FIFTH AMENDED AND RESTATED  
CERTIFICATE OF INCORPORATION**

FIFTH AMENDED AND RESTATED  
CERTIFICATE OF INCORPORATION  
OF  
PROTEON THERAPEUTICS, INC.  
(Pursuant to Sections 242 and 245 of the  
General Corporation Law of the State of Delaware)

Proteon Therapeutics, Inc., a corporation organized and existing under and by virtue of the provisions of the General Corporation Law of the State of Delaware (the “**General Corporation Law**”),

**DOES HEREBY CERTIFY:**

1. That the name of this corporation is Proteon Therapeutics, Inc. The date of filing of the original certificate of incorporation of this corporation with the secretary of state of the State of Delaware was on March 24, 2006.

2. That the Board of Directors duly adopted resolutions proposing to amend and restate the Fourth Amended and Restated Certificate of Incorporation of this corporation (as previously amended and in effect prior to the effective date of this Fifth Amended and Restated Certificate of Incorporation, the “**Prior Charter**”) declaring said amendment and restatement to be advisable and in the best interests of this corporation and its stockholders, and authorizing the appropriate officers of this corporation to solicit the consent of the stockholders therefor

3. This Fifth Amended and Restated Certificate of Incorporation further amends and restates and integrates the Prior Charter to read in its entirety as follows:

**FIRST:** The name of this corporation is Proteon Therapeutics, Inc. (the “**Corporation**”).

**SECOND:** The address of the registered office of the Corporation in the State of Delaware is 1209 Orange Street, in the City of Wilmington, County of New Castle. The name of its registered agent at such address is The Corporation Trust Company.

**THIRD:** The nature of the business or purposes to be conducted or promoted is to engage in any lawful act or activity for which corporations may be organized under the General Corporation Law.

**FOURTH:** The total number of shares of all classes of stock which the Corporation shall have authority to issue is (i) 205,926,290 shares of Common Stock, \$0.001 par value per share (“**Common Stock**”), and (ii) 158,642,302 shares of Preferred Stock, \$0.001 par value per share (“**Preferred Stock**”).

The following is a statement of the designations and the powers, privileges and rights, and the qualifications, limitations or restrictions thereof in respect of each class of capital stock of the Corporation and each series thereof.

**A. COMMON STOCK**

1. General. The voting, dividend and liquidation rights of the holders of the Common Stock are subject to and qualified by the rights, powers and preferences of the holders of the Preferred Stock set forth herein.

2. Voting. The holders of the Common Stock are entitled to one vote for each share of Common Stock held at all meetings of stockholders (and written actions in lieu of meetings); provided, however, that, except as otherwise required by law, holders of Common Stock, as such, shall not be entitled to vote on any amendment to the Certificate of Incorporation that relates solely to the terms of one or more outstanding series of Preferred Stock if the holders of such affected series are entitled, either separately or together with the holders of one or more other such series, to vote thereon pursuant to the Certificate of Incorporation or pursuant to the General Corporation Law. There shall be no cumulative voting. The number of authorized shares of Common Stock may be increased or decreased (but not below the number of shares thereof then outstanding) by (in addition to any vote of the holders of one or more series of Preferred Stock that may be required by the terms of the Certificate of Incorporation) the affirmative vote of the holders of shares of capital stock of the Corporation representing a majority of the votes represented by all outstanding shares of capital stock of the Corporation entitled to vote, irrespective of the provisions of Section 242(b)(2) of the General Corporation Law.

**B. PREFERRED STOCK**

1. Issuance and Reissuance.

Preferred Stock may be issued from time to time in one or more series, each of such series to consist of such number of shares and to have such terms, rights, powers and preferences, and the qualifications and limitations with respect thereto, as stated or expressed herein.

**C. DESIGNATED PREFERRED STOCK**

22,638,465 shares of the authorized Preferred Stock are hereby designated “**Series A Preferred Stock**”, 10,909,091 shares of the authorized Preferred Stock are hereby designated “**Series A-1 Preferred Stock**”, 20,754,461 shares of the authorized Preferred Stock are hereby designated “**Series B Preferred Stock**”, 17,550,758 shares of the authorized Preferred Stock are hereby designated “**Series C Preferred Stock**” and 86,789,527 shares of the authorized Preferred Stock are hereby designated “**Series D Preferred Stock**” with the following rights, preferences, powers, privileges and restrictions, qualifications and limitations. The Series



A Preferred Stock, Series A-1 Preferred Stock, Series B Preferred Stock, Series C Preferred Stock and Series D Preferred Stock are collectively referred to as the “**Designated Preferred Stock.**” Unless otherwise indicated, references to “Sections” or “Subsections” in this Part C of this Article Fourth refer to sections and subsections of Part C of this Article Fourth.

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## 1. Dividends.

1.1 From and after the Series D Original Issue Date, dividends at the rate per annum of \$0.07 per share shall accrue on such shares of Series A Preferred Stock (in each case subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization affecting such shares) (the “**Series A Accruing Dividends**”). From and after the Series D Original Issue Date, dividends at the rate per annum of \$0.077 per share shall accrue on such shares of Series A-1 Preferred Stock (in each case subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization affecting such shares) (the “**Series A-1 Accruing Dividends**”). From and after the Series D Original Issue Date, dividends at the rate per annum of \$0.0805 per share shall accrue on such shares of Series B Preferred Stock (in each case subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization affecting such shares) (the “**Series B Accruing Dividends**”). From and after the Series D Original Issue Date, dividends at the rate per annum of \$0.0805 per share shall accrue on such shares of Series C Preferred Stock (in each case subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization affecting such shares) (the “**Series C Accruing Dividends**”). From and after the date of the issuance of any shares of Series D Preferred Stock, dividends at the rate per annum of \$0.0412 per share shall accrue on such shares of Series D Preferred Stock (in each case subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization affecting such shares) (the “**Series D Accruing Dividends**” and together with the Series A Accruing Dividends, the Series A-1 Accruing Dividends, Series B Accruing Dividends and Series C Accruing Dividends, the “**Accruing Dividends**”). Accruing Dividends shall accrue from day to day, whether or not declared, and shall be cumulative; provided however, that the Accruing Dividends shall not be payable except as set forth in Section 6.

1.2 The holders of Designated Preferred Stock, in preference to the holders of Common Stock, shall be entitled to receive, when and as declared by the Board of Directors of the Corporation (the “**Board of Directors**”), but only out of funds that are legally available therefor, cash dividends at the rate of (i) in the case of the Series A Preferred Stock, seven percent (7%) of the Series A Original Issue Price (as defined below) per annum on each outstanding share of Series A Preferred Stock, (ii) in the case of the Series A-1 Preferred Stock, seven percent (7%) of the Series A-1 Original Issue Price (as defined below) per annum on each outstanding share of Series A-1 Preferred Stock, (iii) in the case of the Series B Preferred Stock, seven percent (7%) of the Series B Original Issue Price (as defined below) per annum on each outstanding share of Series B Preferred Stock, (iv) in the case of the Series C Preferred Stock, seven percent (7%) of the Series C Original Issue Price (as defined below) per annum on each outstanding share of Series C Preferred Stock and (v) in the case of the Series D Preferred Stock, seven percent (7%) of the Series D Original Issue Price (as defined below) per annum on each outstanding share of Series D Preferred Stock (in each case, as adjusted for any stock dividends, combinations, splits, recapitalizations and the like with respect to such shares after the filing date hereof). Such dividends shall be payable only when, as and if declared by the Board of Directors and shall be non-cumulative.

1.3 The Corporation shall not declare, pay or set aside any dividends on Common Stock (other than dividends on shares of Common Stock payable in shares of Common

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Stock) unless (in addition to the obtaining of any consents required elsewhere in the Certificate of Incorporation) the holders of the Designated Preferred Stock then outstanding shall first receive, or simultaneously receive, a dividend on each outstanding share of Designated Preferred Stock in an amount at least equal to or greater than the product of (1) the dividend payable on each share of Common Stock and (2) the number of shares of Common Stock issuable upon conversion of such share of Designated Preferred Stock calculated on the record date for determination of holders entitled to receive such dividend.

1.4 Except as described in Subsections 1.1, 1.2 and 1.3, the Corporation shall not declare, pay or set aside any dividends on the Series A Preferred Stock, the Series A-1 Preferred Stock, the Series B Preferred Stock or the Series C Preferred Stock unless (in addition to the obtaining of any consents required elsewhere in the Certificate of Incorporation) the holders of the Series D Preferred Stock then outstanding shall first receive, or simultaneously receive, a dividend on each outstanding share of Series D Preferred Stock in an amount at least equal to or greater than (1) in the case of a dividend on the Series A Preferred Stock, the product of (x) the dividend payable on each share of Series A Preferred Stock divided by the number of shares of Common Stock issuable upon conversion of such share of Series A Preferred Stock calculated on the record date for determination of holders entitled to receive such dividend, and (y) the number of shares of Common Stock issuable upon conversion of such share of Series D Preferred Stock calculated on the record date for determination of holders entitled to receive such dividend, (2) in the case of a dividend on the Series A-1 Preferred Stock, the product of (x) the dividend payable on each share of Series A-1 Preferred Stock divided by the number of shares of Common Stock issuable upon conversion of such share of Series A-1 Preferred Stock calculated on the record date for determination of holders entitled to receive such dividend, and (y) the number of shares of Common Stock issuable upon conversion of such share of Series D Preferred Stock calculated on the record date for determination of holders entitled to receive such dividend, (3) in the case of a dividend on the Series B Preferred Stock, the product of (x) the dividend payable on each share of Series B Preferred Stock divided by the number of shares of Common Stock issuable upon conversion of such share of Series B Preferred Stock calculated on the record date for determination of holders entitled to receive such dividend and (y) the number of shares of Common Stock issuable upon conversion of such share of Series D Preferred Stock calculated on the record date for determination of holders entitled to receive such dividend and (4) in the case of a dividend on the Series C Preferred Stock, the product of (x) the dividend payable on each share of Series C Preferred Stock divided by the number of shares of Common Stock issuable upon conversion of such share of Series C Preferred Stock calculated on the record date for determination of holders entitled to receive such dividend and (y) the number of shares of Common Stock issuable upon conversion of such share of Series D Preferred Stock calculated on the record date for determination of holders entitled to receive such dividend.

1.5 Except as described in Subsections 1.1, 1.2, 1.3 and 1.4, the Corporation shall not declare, pay or set aside any dividends on the Series A Preferred Stock or the Series A-1 Preferred Stock unless (in addition to the obtaining of any consents required elsewhere in the Certificate of Incorporation) the holders of the Series B Preferred Stock then outstanding shall first receive, or simultaneously receive, a dividend on each outstanding share of Series B Preferred Stock in an amount at least equal to or greater than (1) in the case of a dividend on the Series A Preferred Stock, the product of (x) the dividend payable on each share of Series A Preferred Stock divided by the number of shares of Common Stock issuable upon conversion of

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such share of Series A Preferred Stock calculated on the record date for determination of holders entitled to receive such dividend, and (y) the number of shares of Common Stock issuable upon conversion of such share of Series B Preferred Stock, calculated on the record date for determination of holders entitled to receive such dividend, and (2) in the case of a dividend on the Series A-1 Preferred Stock, the product of (x) the dividend payable on each share of Series A-1 Preferred Stock divided by the number of shares of Common Stock issuable upon conversion of such share of Series A-1 Preferred Stock calculated on the record date for

determination of holders entitled to receive such dividend, and (y) the number of shares of Common Stock issuable upon conversion of such share of Series B Preferred Stock, calculated on the record date for determination of holders entitled to receive such dividend.

1.6 The “**Series A Original Issue Price**” shall mean \$1.00 per share, subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Series A Preferred Stock.

1.7 The “**Series A-1 Original Issue Price**” shall mean \$1.10 per share, subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Series A-1 Preferred Stock.

1.8 The “**Series B Original Issue Price**” shall mean \$1.15 per share, subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Series B Preferred Stock.

1.9 The “**Series C Original Issue Price**” shall mean \$1.15 per share, subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Series C Preferred Stock.

1.10 The “**Series D Original Issue Price**” shall mean \$0.588656 per share, subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Series D Preferred Stock.

## 2. Liquidation, Dissolution or Winding Up; Certain Mergers, Consolidations and Asset Sales.

### 2.1 Preferential Payments to Holders of Designated Preferred Stock.

2.1.1 Series D Preferred Stock Liquidation Preference. In the event of any voluntary or involuntary liquidation, dissolution or winding up of the Corporation, the holders of shares of Series D Preferred Stock then outstanding shall be entitled to be paid first out of the assets of the Corporation available for distribution to its stockholders before any payment shall be made to the holders of Series C Preferred Stock, Series B Preferred Stock, Series A-1 Preferred Stock, Series A Preferred Stock or Common Stock by reason of their ownership thereof, an amount per share equal to the Series D Liquidation Price, together with any dividends declared but unpaid thereon (but specifically excluding any Accruing Dividends) (the “**Series D Liquidation Preference**”). If upon any such liquidation, dissolution or winding up of the Corporation, the assets of the Corporation available for distribution to its stockholders shall be insufficient to pay the holders of shares of Series D Preferred Stock the full amount to

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which they shall be entitled under this Subsection 2.1.1, the holders of shares of Series D Preferred Stock shall share ratably in any distribution of the assets available for distribution in proportion to the respective amounts which would otherwise be payable in respect of the shares of Series D Preferred Stock held by them upon such distribution if all amounts payable on or with respect to such shares were paid in full. The “**Series D Liquidation Price**” shall mean \$0.588656 per share, subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Series D Preferred Stock.

2.1.2 Series C Preferred Stock Liquidation Preference. In the event of any voluntary or involuntary liquidation, dissolution or winding up of the Corporation, after payment to the holders of Series D Preferred Stock of the full Series D Liquidation Preference, the holders of shares of Series C Preferred Stock then outstanding shall be entitled to be paid out of the remaining assets of the Corporation available for distribution to its stockholders before any payment shall be made to the holders of Series B Preferred, Series A-1 Preferred Stock, Series A Preferred Stock or Common Stock by reason of their ownership thereof, an amount per share equal to the Series C Liquidation Price, together with any dividends declared but unpaid thereon (but specifically excluding any Accruing Dividends) (the “**Series C Liquidation Preference**”). If upon any such liquidation, dissolution or winding up of the Corporation, after payment to the holders of Series D Preferred Stock of the full Series D Liquidation Preference, the remaining assets of the Corporation available for distribution to its stockholders shall be insufficient to pay the holders of shares of Series C Preferred Stock the full amount to which they shall be entitled under this Subsection 2.1.2, the holders of shares of Series C Preferred Stock shall share ratably in any distribution of the assets available for distribution in proportion to the respective amounts which would otherwise be payable in respect of the shares of Series C Preferred Stock held by them upon such distribution if all amounts payable on or with respect to such shares were paid in full. The “**Series C Liquidation Price**” shall mean \$0.6242 per share, subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Series C Preferred Stock

2.1.3 Series B Preferred Stock Liquidation Preference. In the event of any voluntary or involuntary liquidation, dissolution or winding up of the Corporation, after payment to the holders of Series D Preferred Stock of the full Series D Liquidation Preference and after payment to the holders of Series C Preferred Stock of the full Series C Liquidation Preference, the holders of shares of Series B Preferred Stock then outstanding shall be entitled to be paid out of the remaining assets of the Corporation available for distribution to its stockholders before any payment shall be made to the holders of Series A-1 Preferred Stock, Series A Preferred Stock or Common Stock by reason of their ownership thereof, an amount per share equal to the Series B Liquidation Price, together with any dividends declared but unpaid thereon (but specifically excluding any Accruing Dividends) (the “**Series B Liquidation Preference**”). If upon any such liquidation, dissolution or winding up of the Corporation, after payment to the holders of Series D Preferred Stock of the full Series D Liquidation Preference and after payment to the holders of Series C Preferred Stock of the full Series C Liquidation Preference, the remaining assets of the Corporation available for distribution to its stockholders shall be insufficient to pay the holders of shares of Series B Preferred Stock the full amount to which they shall be entitled under this Subsection 2.1.3, the holders of shares of Series B Preferred Stock shall share ratably in any distribution of the assets available for distribution in proportion to the respective amounts which would otherwise be payable in respect of the shares

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of Series B Preferred Stock held by them upon such distribution if all amounts payable on or with respect to such shares were paid in full. The “**Series B Liquidation Price**” shall mean \$0.6242 per share, subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Series B Preferred Stock

2.1.4 Series A-1 Preferred Stock and Series A Preferred Stock Liquidation Preference. In the event of any voluntary or involuntary liquidation, dissolution or winding up of the Corporation, after payment to the holders of Series D Preferred Stock of the full Series D Liquidation Preference, after payment to the holders of Series C Preferred Stock of the full Series C Liquidation Preference and after payment to the holders of Series B Preferred Stock of the full Series B Liquidation Preference, the holders of shares of Series A-1 Preferred Stock and Series A Preferred Stock then outstanding shall be entitled to be paid out of the remaining assets of the Corporation available for distribution to its stockholders before any payment shall be made to the holders of Common Stock by reason of their ownership thereof, an amount per share equal to (i) in the case of the Series A-1 Preferred Stock, the Series A-1 Liquidation Price, together with any dividends declared but unpaid thereon (but specifically excluding any Accruing Dividends) and (ii) in the case of the Series A Preferred Stock, the Series A Liquidation Price, together with any dividends declared but unpaid thereon (but specifically excluding any Accruing Dividends). If upon any such liquidation, dissolution or winding

up of the Corporation, after payment to the holders of Series D Preferred Stock of the full Series D Liquidation Preference, after payment to the holders of Series C Preferred Stock of the full Series C Liquidation Preference and after payment to the holders of Series B Preferred Stock of the full Series B Liquidation Preference, the remaining assets of the Corporation available for distribution to its stockholders shall be insufficient to pay the holders of shares of Series A-1 Preferred Stock and the holders of shares of Series A Preferred Stock the full amount to which they shall be entitled under this Subsection 2.1.4, the holders of shares of Series A-1 Preferred Stock and the holders of shares of Series A Preferred Stock shall share ratably in any distribution of the remaining assets available for distribution in proportion to the respective amounts which would otherwise be payable in respect of the shares of Series A-1 Preferred Stock and shares of Series A Preferred Stock held by them upon such distribution if all amounts payable on or with respect to such shares were paid in full. The “**Series A-1 Liquidation Price**” shall mean \$0.5971 per share, subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Series A-1 Preferred Stock. The “**Series A Liquidation Price**” shall mean \$0.5428 per share, subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization with respect to the Series A Preferred Stock

2.2 Distribution of Remaining Assets. In the event of any voluntary or involuntary liquidation, dissolution or winding up of the Corporation, after the payment of all preferential amounts required to be paid to the holders of shares of Designated Preferred Stock, the remaining assets of the Corporation available for distribution to its stockholders shall be distributed among the holders of the shares of Designated Preferred Stock and Common Stock, pro rata based on the number of shares held by each such holder, treating for this purpose all such securities as if they had been converted to Common Stock pursuant to the terms of the Certificate of Incorporation immediately prior to such dissolution, liquidation or winding up of the Corporation. The aggregate amount which a holder of a share of Series A Preferred Stock is entitled to receive under Subsections 2.1.4 and 2.2 is hereinafter referred to as the “**Series A**

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**Liquidation Amount**”, the aggregate amount which a holder of a share of Series A-1 Preferred Stock is entitled to receive under Subsections 2.1.4 and 2.2 is hereinafter referred to as the “**Series A-1 Liquidation Amount**”, the aggregate amount which a holder of a share of Series B Preferred Stock is entitled to receive under Subsections 2.1.3 and 2.2 is hereinafter referred to as the “**Series B Liquidation Amount**”, the aggregate amount which a holder of a share of Series C Preferred Stock is entitled to receive under Subsections 2.1.2 and 2.2 is hereinafter referred to as the “**Series C Liquidation Amount**” and the aggregate amount which a holder of a share of Series D Preferred Stock is entitled to receive under Subsections 2.1.1 and 2.2 is hereinafter referred to as the “**Series D Liquidation Amount**.”

### 2.3 Deemed Liquidation Events.

2.3.1 Definition. Each of the following events shall be considered a “**Deemed Liquidation Event**” unless the holders of outstanding shares of Designated Preferred Stock representing at least eighty percent (80%) of the then outstanding shares of Designated Preferred Stock, voting together as a single class on an as converted to Common Stock basis, elect otherwise by written notice sent to the Corporation at least one (1) business day prior to the effective date of any such event:

- (a) a merger or consolidation in which
  - (i) the Corporation is a constituent party or
  - (ii) a subsidiary of the Corporation is a constituent party and the Corporation issues shares of its capital stock pursuant to such merger or consolidation,

except any such merger or consolidation involving the Corporation or a subsidiary in which the shares of capital stock of the Corporation outstanding immediately prior to such merger or consolidation continue to represent, or are converted into or exchanged for shares of capital stock that represent, immediately following such merger or consolidation, a majority, by voting power, of the capital stock of (1) the surviving or resulting corporation or (2) if the surviving or resulting corporation is a wholly owned subsidiary of another corporation immediately following such merger or consolidation, the parent corporation of such surviving or resulting corporation (provided that, for the purpose of this Subsection 2.3.1, all shares of Common Stock issuable upon exercise of Options (as defined below) outstanding immediately prior to such merger or consolidation or upon conversion of Convertible Securities (as defined below) outstanding immediately prior to such merger or consolidation shall be deemed to be outstanding immediately prior to such merger or consolidation and, if applicable, converted or exchanged in such merger or consolidation on the same terms as the actual outstanding shares of Common Stock are converted or exchanged); or

- (b) the sale, lease, transfer, exclusive license or other disposition, in a single transaction or series of related transactions, by the Corporation or any subsidiary of the Corporation of all or substantially all the assets of the Corporation and its subsidiaries taken as a whole, or the sale or disposition (whether by merger or otherwise) of one or more subsidiaries of the Corporation if substantially all of the assets of the Corporation and its

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subsidiaries taken as a whole are held by such subsidiary or subsidiaries, except where such sale, lease, transfer, exclusive license or other disposition is to a wholly owned subsidiary of the Corporation.

The term “**Major Holder**” means a holder of Designated Preferred Stock who together with its Affiliates (as hereinafter defined) holds at least 2,000,000 shares of Designated Preferred Stock (subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization affecting such shares).

The term “**Affiliate**” means with respect to any individual, firm, corporation, partnership, association, limited liability company, trust or any other entity (each, a “**Person**”), any other Person who or which, directly or indirectly, controls, is controlled by or is under common control with such specified Person, including, without limitation, any partner, officer, director, member or employee of such Person and any venture capital fund now or hereafter existing that is controlled by or under common control with one or more general partners of, or shares the same management company with, such Person.

#### 2.3.2 Effecting a Deemed Liquidation Event.

- (a) The Corporation shall not have the power to effect a Deemed Liquidation Event referred to in Subsection 2.3.1(a)(i) above unless the agreement or plan of merger or consolidation for such transaction (the “**Merger Agreement**”) provides that the consideration payable to the stockholders of the Corporation shall be allocated among the holders of capital stock of the Corporation in accordance with Subsections 2.1 and 2.2 above.

- (b) In the event of a Deemed Liquidation Event referred to in Subsection 2.3.1(a)(ii) or 2.3.1(b) above, if the Corporation does not effect a dissolution of the Corporation under the General Corporation Law within ninety (90) calendar days after such Deemed Liquidation Event, then (i) the Corporation shall send a written notice to each holder of Designated Preferred Stock no later than the 90<sup>th</sup> calendar day after the Deemed Liquidation Event

advising such holders of their right (and the requirements to be met to secure such right) pursuant to the terms of the following clause (ii) to require the redemption of such shares of Designated Preferred Stock, and (ii) if the holders of outstanding shares of Designated Preferred Stock representing at least eighty percent (80%) of the then outstanding shares of Designated Preferred Stock, voting together as a single class on an as converted to Common Stock basis, so request in a written instrument delivered to the Corporation not later than 120 calendar days after such Deemed Liquidation Event, the Corporation shall use the consideration received by the Corporation for such Deemed Liquidation Event (net of any retained liabilities associated with the assets sold or technology licensed, as determined in good faith by the Board of Directors) (the “**Net Proceeds**”), to the extent legally available therefor, on the 150<sup>th</sup> calendar day after such Deemed Liquidation Event, to redeem all outstanding shares of Designated Preferred Stock at a price per share equal to (i) in the case of the Series A Preferred Stock, the Series A Liquidation Amount, (ii) in the case of the Series A-1 Preferred Stock, the Series A-1 Liquidation Amount, (iii) in the case of the Series B Preferred Stock, the Series B Liquidation Amount, (iv) in the case of the Series C Preferred Stock, the Series C Liquidation Amount, and (v) in the case of the Series D Preferred Stock, the Series D Liquidation Amount. Notwithstanding the foregoing, in the event of a redemption pursuant to the preceding sentence,

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if the Net Proceeds are not sufficient to redeem all outstanding shares of Designated Preferred Stock, or if the Corporation does not have sufficient legally available funds to effect such redemption, the Corporation shall redeem first a pro rata portion of each holder’s shares of Series D Preferred Stock, if any (in accordance with the relative priorities or preferences of the Series D Preferred Stock), to the fullest extent of such Net Proceeds or such legally available funds, as the case may be, based on the respective amounts which would otherwise be payable in respect of the shares of Series D Preferred Stock, to be redeemed if the Net Proceeds and legally available funds were sufficient to redeem all such shares, and shall redeem the remaining shares of Series D Preferred Stock, to have been redeemed as soon as practicable after the Corporation has funds legally available therefor; second, a pro rata portion of each holder’s shares of Series C Preferred Stock, to the fullest extent of such Net Proceeds or such legally available funds, as the case may be, based on the respective amounts which would otherwise be payable in respect of the shares of Series C Preferred Stock to be redeemed if the Net Proceeds and legally available funds were sufficient to redeem all such shares, and shall redeem the remaining shares of Series C Preferred Stock to have been redeemed as soon as practicable after the Corporation has funds legally available therefor; third, a pro rata portion of each holder’s shares of Series B Preferred Stock, to the fullest extent of such Net Proceeds or such legally available funds, as the case may be, based on the respective amounts which would otherwise be payable in respect of the shares of Series B Preferred Stock to be redeemed if the Net Proceeds and legally available funds were sufficient to redeem all such shares, and shall redeem the remaining shares of Series B Preferred Stock to have been redeemed as soon as practicable after the Corporation has funds legally available therefor; and fourth, a pro rata portion of each holder’s shares of Series A Preferred Stock and Series A-1 Preferred Stock to the fullest extent of the remaining amount of such Net Proceeds or such legally available funds, as the case may be, based on the respective amounts which would otherwise be payable in respect of the shares of Series A Preferred Stock and Series A-1 Preferred Stock to be redeemed if the remaining amount of such Net Proceeds and legally available funds were sufficient to redeem all such shares, and shall redeem the remaining shares to have been redeemed as soon as practicable after the Corporation has funds legally available therefor. The provisions of Subsections 6.2 through 6.4 below shall apply, with such necessary changes in the details thereof as are necessitated by the context, to the redemption of the Designated Preferred Stock pursuant to this Subsection 2.3.2(b). Prior to the distribution or redemption provided for in this Subsection 2.3.2(b), the Corporation shall not expend or dissipate the consideration received for such Deemed Liquidation Event, except to discharge expenses incurred in connection with such Deemed Liquidation Event or in the ordinary course of business.

2.3.3 Amount Deemed Paid or Distributed. The amount deemed paid or distributed to the holders of capital stock of the Corporation upon any such merger, consolidation, sale, transfer, exclusive license, other disposition or redemption shall be the cash or the value of the property, rights or securities paid or distributed to such holders by the Corporation or the acquiring person, firm or other entity. The value of such property, rights or securities shall be determined in good faith by the Board of Directors.

2.3.4 Allocation of Escrow. In the case of a Deemed Liquidation Event pursuant to Subsection 2.3.1(a)(i) above, if any portion of the consideration payable to the stockholders of the Corporation is placed into escrow and/or is payable to the stockholders of the Corporation subject to contingencies, the Merger Agreement shall provide that (a) the portion of

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such consideration that is not placed in escrow and not subject to any contingencies (the “**Initial Consideration**”) shall be allocated among the holders of capital stock of the Corporation in accordance with Subsections 2.1 and 2.2 above as if the Initial Consideration were the only consideration payable in connection with such Deemed Liquidation Event and (b) any additional consideration which becomes payable to the stockholders of the Corporation upon release from escrow or satisfaction of contingencies shall be allocated among the holders of capital stock of the Corporation in accordance with Subsections 2.1 and 2.2 above after taking into account the previous payment of the Initial Consideration as part of the same transaction. The result of this approach is that, for certain transactions, the portion of the transaction consideration that is subject to an escrow or other contingencies may be allocated disproportionately to the holders of Common Stock.

### 3. Voting.

3.1 General. On any matter presented to the stockholders of the Corporation for their action or consideration at any meeting of stockholders of the Corporation (or by written consent of stockholders in lieu of meeting), each holder of outstanding shares of Designated Preferred Stock shall be entitled to cast the number of votes equal to the number of whole shares of Common Stock into which the shares of Designated Preferred Stock held by such holder are convertible as of the record date for determining stockholders entitled to vote on such matter. Except as provided by law or by the other provisions of the Certificate of Incorporation, holders of Designated Preferred Stock shall vote together with the holders of Common Stock as a single class.

#### 3.2 Election of Directors.

(a) The number of directors constituting the whole Board of Directors shall be no less than five (5) and no greater than nine (9).

(b) The holders of record of the shares of Series A Preferred Stock and Series A-1 Preferred Stock, exclusively and voting together as a single class, shall be entitled to elect three (3) directors of the Corporation (the “**Series A/A-1 Directors**”). Any director elected as provided in the preceding sentence may be removed without cause by, and only by, the affirmative vote of the holders of record of the shares of Series A Preferred Stock and Series A-1 Preferred Stock, exclusively and voting together as a single class, given either at a special meeting of such stockholders duly called for that purpose or pursuant to a written consent of stockholders.

(c) The holders of record of the shares of Series B Preferred Stock, exclusively, shall be entitled to elect one (1) director of the Corporation (the “**Series B Director**”). Any director elected as provided in the preceding sentence may be removed without cause by, and only by, the affirmative vote of the holders of record of the shares of Series B Preferred Stock, exclusively, given either at a special meeting of such stockholders duly called for that purpose or pursuant to a written consent of stockholders.

- (d) The holders of record of the shares of Series D Preferred Stock, exclusively, shall be entitled to elect two (2) directors of

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**Directors**”, and together with the Series A/A-1 Directors and the Series B Director, the “**Designated Preferred Directors**”). Any director elected as provided in the preceding sentence may be removed without cause by, and only by, the affirmative vote of the holders of record of the shares of Series D Preferred Stock, exclusively, given either at a special meeting of such stockholders duly called for that purpose or pursuant to a written consent of stockholders.

(e) The holders of record of the shares of Common Stock and Designated Preferred Stock, exclusively and voting together as a single class, shall be entitled to elect the balance of the total number of directors of the Corporation.

(f) At any meeting held for the purpose of electing a director, the presence in person or by proxy of the holders of a majority of the then outstanding shares of the class or series entitled to elect such director shall constitute a quorum for the purpose of electing such director. A vacancy in any directorship filled by the holders of any class or series shall be filled only by vote or written consent in lieu of a meeting of the holders of such class or series or by any remaining director or directors elected by the holders of such class or series pursuant to this Subsection 3.2.

3.3 Designated Preferred Stock Protective Provisions. At any time when shares of Designated Preferred Stock are outstanding, the Corporation shall not, either directly or indirectly by amendment, merger, consolidation or otherwise, do any of the following without (in addition to any other vote required by law or the Certificate of Incorporation) the written consent or affirmative vote of the holders of outstanding shares of Designated Preferred Stock representing at least eighty percent (80%) of the then outstanding shares of Designated Preferred Stock, voting together as a single class on an as converted to Common Stock basis, given in writing or by vote at a meeting:

(a) liquidate, dissolve or wind-up the business and affairs of the Corporation, effect any Deemed Liquidation Event, sell all or any substantial portion of its assets, or consent to any of the foregoing;

(b) amend, alter or repeal any provision of the Certificate of Incorporation or Bylaws of the Corporation (including any filing of a Certificate of Designation or by merger, consolidation, or otherwise);

(c) create, or authorize the creation of, or issue or obligate itself to issue shares of, any additional class or series of capital stock unless the same ranks junior to the Designated Preferred Stock with respect to the distribution of assets on the liquidation, dissolution or winding up of the Corporation, the payment of dividends and redemption rights, or increase the authorized number of shares of Designated Preferred Stock, increase or decrease the number of shares of Preferred Stock designated as Series A Preferred Stock, Series A-1 Preferred Stock, Series B Preferred Stock, Series C Preferred Stock or Series D Preferred Stock or increase the authorized number of shares of any additional class or series of capital stock unless the same ranks junior to the Designated Preferred Stock with respect to the distribution of assets on the liquidation, dissolution or winding up of the Corporation, the payment of dividends and redemption rights;

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(d) purchase or redeem (or permit any subsidiary to purchase or redeem) or pay or declare any dividend or make any distribution on, any shares of capital stock of the Corporation other than (i) redemptions of or dividends or distributions on the Designated Preferred Stock as expressly authorized herein, (ii) dividends or other distributions payable on the Common Stock solely in the form of additional shares of Common Stock and (iii) repurchases of stock from former employees, officers, directors, consultants or other persons who performed services for the Corporation or any subsidiary in connection with the cessation of such employment or service at the lower of the original purchase price or the then current fair market value thereof;

(e) create, or authorize the creation of, or issue, or authorize the issuance of any debt security, or permit any subsidiary to take any such action with respect to any debt security, if the aggregate indebtedness of the Corporation and its subsidiaries for borrowed money following such action would exceed \$3,000,000 unless such debt security has received the prior approval of the Board of Directors, including the approval of a majority of the Designated Preferred Directors;

(f) create, or authorize the creation of, any individual non-debt financial commitment or liability in excess of \$3,000,000, including, without limitation, property leases or long term contracts, unless such non-debt financial commitment or liability has received the prior approval of the Board of Directors, including the approval of a majority of the Designated Preferred Directors;

(g) increase or decrease the authorized number of directors constituting the Board of Directors;

(h) increase or decrease the number of shares reserved for issuance under any stock or option plan of the Corporation, including the Corporation’s 2006 Employee Stock Incentive Plan (as amended and in effect from time to time), or establish any new such stock or option plan; or

(i) change the principal business of the Corporation or exit the current line of business.

#### 4. Optional Conversion.

The holders of the Designated Preferred Stock shall have conversion rights as follows (the “**Conversion Rights**”):

##### 4.1 Right to Convert.

4.1.1 Conversion Ratio. Each share of Designated Preferred Stock shall be convertible, at the option of the holder thereof, at any time and from time to time, and without the payment of additional consideration by the holder thereof, into such number of fully paid and nonassessable shares of Common Stock as is determined by dividing (i) in the case of the Series A Preferred Stock, the Series A Original Issue Price by the Series A Conversion Price (as defined below) in effect at the time of conversion, (ii) in the case of the Series A-1 Preferred Stock, the Series A-1 Original Issue Price by the Series A-1 Conversion Price (as defined below)

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in effect at the time of conversion, (iii) in the case of the Series B Preferred Stock, the Series B Original Issue Price by the Series B Conversion Price (as defined below) and (iv) in the case of the Series C Preferred Stock, the Series C Original Issue Price by the Series C Conversion Price (as defined below) and (v) in the case of the Series D Preferred Stock, the Series D Original Issue Price by the Series D Conversion Price (as defined below). The “**Series A Conversion Price**” shall initially be equal to \$0.8388. The “**Series A-1 Conversion Price**” shall initially be equal to \$0.9022. The “**Series B Conversion Price**” shall initially be equal to \$0.9339. The “**Series C Conversion Price**” shall initially be equal to \$0.9339. The “**Series D Conversion Price**” shall initially be equal to \$0.5887. Such initial Series A Conversion Price, Series A-1 Conversion Price, Series B Conversion Price, Series C Conversion Price and Series D Conversion Price, and the rate at which shares of Series A Preferred Stock, Series A-1 Preferred Stock, Series B Preferred Stock, Series C Preferred Stock and Series D Preferred Stock may be converted into shares of Common Stock, shall be subject to adjustment as provided below.

4.1.2 Incremental Conversion. In the event that,

(a) the Corporation consummates the sale of shares of Common Stock to the public in the Corporation’s first underwritten public offering pursuant to an effective registration statement under the Securities Act of 1933, as amended (the “**IPO**”),

(b) any holder of shares of Series D Preferred Stock that, immediately prior to the closing of the IPO, is contractually entitled to purchase shares of Series D Preferred Stock pursuant to the Series D Purchase Agreement (as defined in Subsection 4.4.1 hereof) upon exercise of such holder’s Second Tranche Individual Purchase Right (as defined in the Series D Purchase Agreement) or Third Tranche Individual Purchase Right (as defined in the Series D Purchase Agreement) (assuming, for purposes of this clause (b), that the restrictions set forth in the Series D Purchase Agreement with respect to purchasing shares of Series D Preferred Stock during the Restricted Period (as defined in the Series D Purchase Agreement) are not applicable),

(c) such holder referred to in clause (b) above is offered the opportunity to purchase shares of Common Stock in the IPO and such holder purchases shares of Common Stock in the IPO, and

(d) the price per share of Common Stock at which the Corporation sells shares of Common Stock to the public pursuant to the IPO (the “**IPO Price**”) is greater than the Series D Conversion Price in effect immediately prior to the IPO,

then, upon conversion of the shares of Series D Preferred Stock held by such holder immediately prior to the closing of the IPO (regardless of whether such conversion occurs immediately prior to the closing of the IPO or at any time thereafter), each share of Series D Preferred Stock held by such holder immediately prior to the closing of the IPO, when converted into shares of Common Stock in accordance with the provisions of this Section 4, shall, in addition to converting into the number of shares of Common Stock determined in accordance with Subsection 4.1.1 at the conversion rate in effect for the Series D Preferred Stock at the time of such conversion, also convert into an additional number of shares of Common Stock determined by dividing (A) the product of (i) the number of shares of Common Stock purchased in the IPO

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by such holder up to a maximum number equal to the aggregate number of shares of Common Stock that would be issuable pursuant Subsection 4.1.1 above upon conversion, immediately prior to the closing of the IPO, of the maximum number of shares of Series D Preferred Stock that such holder is contractually entitled to purchase, immediately prior to the closing of the IPO, in accordance with the terms and conditions of the Series D Purchase Agreement upon exercise of such holder’s Second Tranche Individual Purchase Right and/or Third Tranche Individual Purchase Right, as applicable, assuming for purposes of determining such maximum number of shares of Series D Preferred Stock that the restrictions set forth in the Series D Purchase Agreement with respect to purchasing shares of Series D Preferred Stock during the Restricted Period are not applicable and assuming for purposes of this clause (i) that such holder purchased and held such maximum number of shares of Series D Preferred Stock immediately prior to the closing of the IPO and (ii) the remainder obtained by subtracting the number 1 from the quotient obtained by dividing the IPO Price by the Series D Conversion Price in effect immediately prior to the closing of the IPO, by (B) the number of shares of Series D Preferred Stock held by such holder immediately prior to the IPO. Notwithstanding the foregoing, the right of such holder to receive any shares of Common Stock pursuant to this Subsection 4.1.2 upon conversion of the shares of Series D Preferred Stock held by such holder immediately prior to the closing of the IPO is subject to, and contingent upon, the Corporation having received reasonable confirmation or verification that such holder purchased shares of Common Stock in the IPO, which reasonable confirmation or verification may include, among other things, written confirmation by the underwriter or underwriters of the IPO that such holder received a particular allocation of shares of Common Stock in the IPO and that such holder has agreed to purchase such shares in the IPO.

4.1.3 Termination of Conversion Rights. In the event of a notice of redemption of any shares of Designated Preferred Stock pursuant to Section 6, the Conversion Rights of the shares designated for redemption shall terminate at the close of business on the last full day preceding the date fixed for redemption, unless the redemption price is not fully paid on such redemption date, in which case the Conversion Rights for such shares shall continue until such price is paid in full. In the event of a liquidation, dissolution or winding up of the Corporation or a Deemed Liquidation Event, the Conversion Rights shall terminate at the close of business on the last full day preceding the date fixed for the payment of any such amounts distributable on such event to the holders of Designated Preferred Stock.

4.2 Fractional Shares. No fractional shares of Common Stock shall be issued upon conversion of the Designated Preferred Stock. In lieu of any fractional shares to which the holder would otherwise be entitled, the Corporation shall pay cash equal to such fraction multiplied by the fair market value of a share of Common Stock as determined in good faith by the Board of Directors. Whether or not fractional shares would be issuable upon such conversion shall be determined on the basis of the total number of shares of Designated Preferred Stock the holder is at the time converting into Common Stock and the aggregate number of shares of Common Stock issuable upon such conversion.

4.3 Mechanics of Conversion.

4.3.1 Notice of Conversion. In order for a holder of Designated Preferred Stock to voluntarily convert shares of Designated Preferred Stock into shares of Common Stock, such holder shall surrender the certificate or certificates for such shares of

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Designated Preferred Stock (or, if such registered holder alleges that such certificate has been lost, stolen or destroyed, a lost certificate affidavit and agreement reasonably acceptable to the Corporation to indemnify the Corporation against any claim that may be made against the Corporation on account of the alleged loss, theft or destruction of such certificate), at the office of the transfer agent for the Designated Preferred Stock (or at the principal office of the Corporation if the Corporation serves as its own transfer agent), together with written notice that such holder elects to convert all or any number of the shares of the Designated Preferred Stock represented by such certificate or certificates and, if applicable, any event on which such conversion is contingent. Such notice shall state such holder’s name or the names of the nominees in which such holder wishes the certificate or certificates for shares of Common Stock to be issued. If required by the Corporation, certificates surrendered for conversion shall be endorsed or accompanied by a written instrument or instruments of transfer, in form satisfactory to the Corporation, duly executed by the registered holder or his, her or its attorney duly authorized in writing. The close of business on the date of the last to occur of (i)

the receipt by the transfer agent (or by the Corporation if the Corporation serves as its own transfer agent) of such certificates (or lost certificate affidavit and agreement) and notice, or (ii) if such conversion is contingent upon the occurrence of any event, the occurrence of such event, shall be the time of conversion (the “**Conversion Time**”), and the shares of Common Stock issuable upon conversion of the shares represented by such certificate shall be deemed to be outstanding of record as of such date. The Corporation shall, as soon as practicable after the Conversion Time, issue and deliver to such holder of Designated Preferred Stock, or to his, her or its nominees, a certificate or certificates for the number of full shares of Common Stock issuable upon such conversion in accordance with the provisions hereof, a certificate for the number (if any) of the shares of Designated Preferred Stock represented by the surrendered certificate that were not converted into Common Stock, and cash as provided in Subsection 4.2 in lieu of any fraction of a share of Common Stock otherwise issuable upon such conversion and payment of any declared but unpaid dividends (but not any undeclared Accruing Dividends) on the shares of Designated Preferred Stock converted.

4.3.2 Reservation of Shares. The Corporation shall at all times when the Designated Preferred Stock shall be outstanding, reserve and keep available out of its authorized but unissued capital stock, for the purpose of effecting the conversion of the Designated Preferred Stock, such number of its duly authorized shares of Common Stock as shall from time to time be sufficient to effect the conversion of all outstanding Designated Preferred Stock; and if at any time the number of authorized but unissued shares of Common Stock shall not be sufficient to effect the conversion of all then outstanding shares of the Designated Preferred Stock, the Corporation shall take such corporate action as may be necessary to increase its authorized but unissued shares of Common Stock to such number of shares as shall be sufficient for such purposes, including, without limitation, engaging in best efforts to obtain the requisite stockholder approval of any necessary amendment to the Certificate of Incorporation. Before taking any action which would cause an adjustment reducing the Series A Conversion Price, Series A-1 Conversion Price, Series B Conversion Price, Series C Conversion Price or Series D Conversion Price below the then par value of the shares of Common Stock issuable upon conversion of the Series A Preferred Stock, Series A-1 Preferred Stock, Series B Preferred Stock, Series C Preferred Stock or Series D Preferred Stock, the Corporation will take any corporate action which may, in the opinion of its counsel, be necessary in order that the Corporation may validly and legally issue fully paid and nonassessable shares of Common Stock at such adjusted

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Series A Conversion Price, Series A-1 Conversion Price, Series B Conversion Price, Series C Conversion Price or Series D Conversion Price.

4.3.3 Effect of Conversion. All shares of Designated Preferred Stock which shall have been surrendered for conversion as herein provided shall no longer be deemed to be outstanding and all rights with respect to such shares shall immediately cease and terminate at the Conversion Time, except only the right of the holders thereof to receive shares of Common Stock in exchange therefor and to receive payment of any dividends declared but unpaid thereon. Any shares of Designated Preferred Stock so converted shall be retired and cancelled and may not be reissued as shares of such series, and the Corporation may thereafter take such appropriate action (without the need for stockholder action) as may be necessary to reduce the authorized number of shares of Designated Preferred Stock accordingly.

4.3.4 No Further Adjustment. Upon any such conversion, no adjustment to the Series A Conversion Price, Series A-1 Conversion Price, Series B Conversion Price, Series C Conversion Price or Series D Conversion Price shall be made for any accrued but unpaid dividends on the Series A Preferred Stock, Series A-1 Preferred Stock, Series B Preferred Stock, Series C Preferred Stock or Series D Preferred Stock surrendered for conversion or on the Common Stock delivered upon conversion.

4.3.5 Taxes. The Corporation shall pay any and all issue and other similar taxes that may be payable in respect of any issuance or delivery of shares of Common Stock upon conversion of shares of Designated Preferred Stock pursuant to this Section 4. The Corporation shall not, however, be required to pay any tax which may be payable in respect of any transfer involved in the issuance and delivery of shares of Common Stock in a name other than that in which the shares of Designated Preferred Stock so converted were registered, and no such issuance or delivery shall be made unless and until the person or entity requesting such issuance has paid to the Corporation the amount of any such tax or has established, to the satisfaction of the Corporation, that such tax has been paid.

#### 4.4 Adjustments to Conversion Price for Diluting Issues.

4.4.1 Special Definitions. For purposes of this Article Fourth, the following definitions shall apply:

(a) **“Convertible Securities”** shall mean any evidences of indebtedness, shares or other securities directly or indirectly convertible into or exchangeable for Common Stock, but excluding Options.

(b) **“Option”** shall mean rights, options or warrants to subscribe for, purchase or otherwise acquire Common Stock or Convertible Securities.

(c) **“Series C Purchase Agreement”** shall mean that certain Series C Preferred Stock and Warrant Purchase Agreement, dated August 2, 2011, by and among the Corporation and the other parties named therein, as amended and in effect from time to time.

(d) **“Series D Original Issue Date”** shall mean the date on which the first share of Series D Preferred Stock was issued.

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(e) **“Series D Purchase Agreement”** shall mean that certain Series D Preferred Stock Purchase Agreement, to be entered into on or about May 13, 2014, by and among the Corporation and the other parties named therein, as amended and in effect from time to time.

(f) **“Warrants”** shall mean the warrants issued pursuant to, and in accordance with, the Series C Purchase Agreement and which are exercisable for shares of Common Stock in accordance with the terms thereof.

(g) **“Additional Shares of Common Stock”** shall mean all shares of Common Stock issued (or, pursuant to Subsection 4.4.3 below, deemed to be issued) by the Corporation after the Series D Original Issue Date, other than the following shares of Common Stock, and shares of Common Stock deemed issued pursuant to the following Options and Convertible Securities (collectively **“Exempted Securities”**):

(i) shares of Common Stock, Options or Convertible Securities issued as a dividend or distribution on Designated Preferred Stock;

(ii) shares of Common Stock, Options or Convertible Securities issued by reason of a dividend, stock split, split-up or other distribution on shares of Common Stock that is covered by Subsection 4.5, 4.6, 4.7 or 4.8 below;

- (iii) shares of Common Stock or Options issued to employees or directors of, or consultants or advisors to, the Corporation or any of its subsidiaries pursuant to a plan, agreement or arrangement approved by the Board of Directors;
  - (iv) shares of Common Stock or Convertible Securities actually issued upon the exercise of Options or shares of Common Stock actually issued upon the conversion or exchange of Convertible Securities, in each case provided such issuance is pursuant to the terms of such Option or Convertible Security;
  - (v) shares of Common Stock, Options or Convertible Securities issued to banks, equipment lessors or other financial institutions, or to real property lessors, pursuant to a debt financing, equipment leasing or real property leasing transaction approved by the Board of Directors including a majority of the Designated Preferred Directors;
  - (vi) shares of Common Stock, Options, or Convertible Securities issued or issuable to a contracting party
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in connection with a licensing, corporate partnering, merger, acquisition or similar strategic or combination transaction approved by a majority of the Board of Directors, including a majority of the Designated Preferred Directors;

- (vii) the Note Conversion Shares (as defined in the Series D Purchase Agreement) and the Initial Tranche Shares (as defined in the Series D Purchase Agreement) issued pursuant to the Series D Purchase Agreement;
  - (viii) each Purchaser's (as defined in the Series D Purchase Agreement) Second Tranche Individual Purchase Right and Third Tranche Individual Purchase Right, and the Series D Preferred Stock or the Common Stock issuable pursuant to the Series D Purchase Agreement upon exercise of such Purchaser's Second Tranche Individual Purchase Right or Third Tranche Individual Purchase Right (it being understood that the foregoing provisions of this clause (viii) shall not be applicable to any Series D Preferred Stock or Common Stock that is actually issued and sold pursuant to the Series D Purchase Agreement upon exercise of such Purchaser's Second Tranche Individual Purchase Right or Third Tranche Individual Purchase Right);
  - (ix) the Common Stock issued or issuable upon conversion of the Series D Preferred Stock issued or issuable pursuant to the Series D Purchase Agreement (including, without limitation, the Common Stock issued or issuable pursuant to Subsection 4.1.2 hereof upon conversion of such Series D Preferred Stock) (it being understood that the foregoing provisions of this clause (ix) shall not be applicable to any Series D Preferred Stock that is actually issued and sold pursuant to the Series D Purchase Agreement at the Second Tranche Closing (as defined in the Series D Purchase Agreement) or the Third Tranche Closing (as defined in the Series D Purchase Agreement)); or
  - (x) the Warrants and/or any shares of Common Stock issued or issuable upon exercise of the Warrants.
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4.4.2 No Adjustment of Conversion Price. No adjustment in the Series A Conversion Price, Series A-1 Conversion Price, Series B Conversion Price, Series C Conversion Price or Series D Conversion Price, as applicable, shall be made as the result of the issuance or deemed issuance of Additional Shares of Common Stock if the Corporation receives written notice from the holders of a majority of the then outstanding shares of Series A Preferred Stock, Series A-1 Preferred Stock, Series B Preferred Stock, or Series C Preferred Stock, or the holders of at least sixty five percent (65%) of the then outstanding shares of Series D Preferred Stock, as applicable, agreeing that no such adjustment to the conversion price of such series shall be made as the result of the issuance or deemed issuance of such Additional Shares of Common Stock.

4.4.3 Deemed Issue of Additional Shares of Common Stock.

(a) If the Corporation at any time or from time to time after the Series D Original Issue Date shall issue any Options or Convertible Securities (excluding Options or Convertible Securities which are themselves Exempted Securities) or shall fix a record date for the determination of holders of any class of securities entitled to receive any such Options or Convertible Securities, then the maximum number of shares of Common Stock (as set forth in the instrument relating thereto, assuming the satisfaction of any conditions to exercisability, convertibility or exchangeability but without regard to any provision contained therein for a subsequent adjustment of such number) issuable upon the exercise of such Options or, in the case of Convertible Securities and Options therefor, the conversion or exchange of such Convertible Securities, shall be deemed to be Additional Shares of Common Stock issued as of the time of such issue or, in case such a record date shall have been fixed, as of the close of business on such record date.

(b) If the terms of any Option or Convertible Security, the issuance of which resulted in an adjustment to the Series A Conversion Price, Series A-1 Conversion Price, Series B Conversion Price, Series C Conversion Price or Series D Conversion Price pursuant to the terms of Subsection 4.4.4 below, are revised as a result of an amendment to such terms or any other adjustment pursuant to the provisions of such Option or Convertible Security (but excluding automatic adjustments to such terms pursuant to anti-dilution or similar provisions of such Option or Convertible Security) to provide for either (1) any increase or decrease in the number of shares of Common Stock issuable upon the exercise, conversion and/or exchange of any such Option or Convertible Security or (2) any increase or decrease in the consideration payable to the Corporation upon such exercise, conversion and/or exchange, then, effective upon such increase or decrease becoming effective, the Series A Conversion Price, Series A-1 Conversion Price, Series B Conversion Price, Series C Conversion Price or Series D Conversion Price, as applicable, computed upon the original issue of such Option or Convertible Security (or upon the occurrence of a record date with respect thereto) shall be readjusted to such Series A Conversion Price, Series A-1 Conversion Price, Series B Conversion Price, Series C Conversion Price or Series D Conversion Price as would have obtained had such revised terms been in effect upon the original date of issuance of such Option or Convertible Security. Notwithstanding the foregoing, no readjustment pursuant to this clause (b) shall have the effect of increasing the Series A Conversion Price, Series A-1 Conversion Price, Series B Conversion Price, Series C Conversion Price or Series D Conversion Price to an amount which exceeds the lower of (i) the Series A Conversion Price, Series A-1 Conversion Price, Series B

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Conversion Price, Series C Conversion Price or Series D Conversion Price, as the case may be, in effect immediately prior to the original adjustment made as a result of the issuance of such Option or Convertible Security, or (ii) the Series A Conversion Price, Series A-1 Conversion Price, Series B Conversion Price, Series C Conversion Price or Series D Conversion Price that would have resulted from any issuances of Additional Shares of Common Stock (other than deemed issuances of Additional Shares of Common Stock as a result of the issuance of such Option or Convertible Security) between the original adjustment date and such readjustment date.

(c) If the terms of any Option or Convertible Security (excluding Options or Convertible Securities which are themselves Exempted Securities), the issuance of which did not result in an adjustment to the Series A Conversion Price, Series A-1 Conversion Price, Series B Conversion Price, Series C Conversion Price or Series D Conversion Price pursuant to the terms of Subsection 4.4.4 below (either because the consideration per share (determined pursuant to Subsection 4.4.5 hereof) of the Additional Shares of Common Stock subject thereto was equal to or greater than the Series A Conversion Price, Series A-1 Conversion Price, Series B Conversion Price, Series C Conversion Price or Series D Conversion Price then in effect, or because such Option or Convertible Security was issued before the Series D Original Issue Date), are revised after the Series D Original Issue Date as a result of an amendment to such terms or any other adjustment pursuant to the provisions of such Option or Convertible Security (but excluding automatic adjustments to such terms pursuant to anti-dilution or similar provisions of such Option or Convertible Security) to provide for either (1) any increase or decrease in the number of shares of Common Stock issuable upon the exercise, conversion or exchange of any such Option or Convertible Security or (2) any increase or decrease in the consideration payable to the Corporation upon such exercise, conversion or exchange, then such Option or Convertible Security, as so amended or adjusted, and the Additional Shares of Common Stock subject thereto (determined in the manner provided in Subsection 4.4.3(a) above) shall be deemed to have been issued effective upon such increase or decrease becoming effective.

(d) Upon the expiration or termination of any unexercised Option or unconverted or unexchanged Convertible Security (or portion thereof) which resulted (either upon its original issuance or upon a revision of its terms) in an adjustment to the Series A Conversion Price, Series A-1 Conversion Price, Series B Conversion Price, Series C Conversion Price or Series D Conversion Price pursuant to the terms of Subsection 4.4.4 below, the Series A Conversion Price, Series A-1 Conversion Price, Series B Conversion Price, Series C Conversion Price or Series D Conversion Price, as applicable, shall be readjusted to such Series A Conversion Price, Series A-1 Conversion Price, Series B Conversion Price, Series C Conversion Price or Series D Conversion Price as would have obtained had such Option or Convertible Security (or portion thereof) never been issued.

(e) If the number of shares of Common Stock issuable upon the exercise, conversion and/or exchange of any Option or Convertible Security, or the consideration payable to the Corporation upon such exercise, conversion and/or exchange, is calculable at the time such Option or Convertible Security is issued or amended but is subject to adjustment based upon subsequent events, any adjustment to the Series A Conversion Price, Series A-1 Conversion Price, Series B Conversion Price, Series C Conversion Price or Series D

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Conversion Price provided for in this Subsection 4.4.3 shall be effected at the time of such issuance or amendment based on such number of shares or amount of consideration without regard to any provisions for subsequent adjustments (and any subsequent adjustments shall be treated as provided in clauses (b) and (c) of this Subsection 4.4.3). If the number of shares of Common Stock issuable upon the exercise, conversion and/or exchange of any Option or Convertible Security, or the consideration payable to the Corporation upon such exercise, conversion and/or exchange, cannot be calculated at all at the time such Option or Convertible Security is issued or amended, any adjustment to the Series A Conversion Price, Series A-1 Conversion Price, Series B Conversion Price, Series C Conversion Price or Series D Conversion Price that would result under the terms of this Subsection 4.4.3 at the time of such issuance or amendment shall instead be effected at the time such number of shares and/or amount of consideration is first calculable (even if subject to subsequent adjustments), assuming for purposes of calculating such adjustment to the Series A Conversion Price, Series A-1 Conversion Price, Series B Conversion Price, Series C Conversion Price or Series D Conversion Price that such issuance or amendment took place at the time such calculation can first be made.

4.4.4 Adjustment of Conversion Price Upon Issuance of Additional Shares of Common Stock. In the event the Corporation shall at any time after the Series D Original Issue Date issue Additional Shares of Common Stock (including Additional Shares of Common Stock deemed to be issued pursuant to Subsection 4.4.3), without consideration or for a consideration per share less than the Series A Conversion Price, Series A-1 Conversion Price, Series B Conversion Price, Series C Conversion Price or Series D Conversion Price in effect immediately prior to such issue, then the Series A Conversion Price, Series A-1 Conversion Price, Series B Conversion Price, Series C Conversion Price or Series D Conversion Price, as the case may be, shall be reduced, concurrently with such issue, to a price (calculated to the nearest one-hundredth of a cent) determined in accordance with the following formula:

$$CP_2 = CP_1 * (A + B) \div (A + C)$$

For purposes of the foregoing formula, the following definitions shall apply:

(a) "CP<sub>2</sub>" shall mean the Series A Conversion Price, Series A-1 Conversion Price, Series B Conversion Price, Series C Conversion Price or Series D Conversion Price, as the case may be, in effect immediately after such issue of Additional Shares of Common Stock;

(b) "CP<sub>1</sub>" shall mean the Series A Conversion Price, Series A-1 Conversion Price, Series B Conversion Price, Series C Conversion Price or Series D Conversion Price, as the case may be, in effect immediately prior to such issue of Additional Shares of Common Stock;

(c) "A" shall mean the number of shares of Common Stock outstanding immediately prior to such issue of Additional Shares of Common Stock (treating for this purpose as outstanding all shares of Common Stock issuable upon exercise of Options outstanding immediately prior to such issue or upon conversion or exchange of Convertible Securities (including the Designated Preferred Stock) outstanding (assuming exercise of any outstanding Options therefor) immediately prior to such issue);

(d) "B" shall mean the number of shares of Common Stock that would have been issued if such Additional Shares of Common Stock had been issued at a price per share equal to CP<sub>1</sub> (determined by dividing the aggregate consideration received by the Corporation in respect of such issue by CP<sub>1</sub>); and

(e) "C" shall mean the number of such Additional Shares of Common Stock issued in such transaction.

4.4.5 Determination of Consideration. For purposes of this Subsection 4.4, the consideration received by the Corporation for the issue of any Additional Shares of Common Stock shall be computed as follows:

(a) Cash and Property. Such consideration shall:

- (i) insofar as it consists of cash, be computed at the aggregate amount of cash received by the Corporation, excluding amounts paid or payable for accrued interest;
- (ii) insofar as it consists of property other than cash, be computed at the fair market value thereof at the time of such issue, as determined in good faith by the Board of Directors; and
- (iii) in the event Additional Shares of Common Stock are issued together with other shares or securities or other assets of the Corporation for consideration which covers both, be the proportion of such consideration so received that is allocated to such Additional Shares of Common Stock, computed as provided in clauses (i) and (ii) above, as determined in good faith by the Board of Directors.

(b) Options and Convertible Securities. The consideration per share received by the Corporation for Additional Shares of Common Stock deemed to have been issued pursuant to Subsection 4.4.3, relating to Options and Convertible Securities, shall be determined by dividing

- (i) the total amount, if any, received or receivable by the Corporation as consideration for the issue of such Options or Convertible Securities, plus the minimum aggregate amount of additional consideration (as set forth in the instruments relating thereto, without regard to any provision contained therein for a subsequent adjustment of such consideration) payable to the Corporation upon the exercise of such Options or the conversion or exchange of such Convertible Securities, or in the

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case of Options for Convertible Securities, the exercise of such Options for Convertible Securities and the conversion or exchange of such Convertible Securities, by

- (ii) the maximum number of shares of Common Stock (as set forth in the instruments relating thereto, without regard to any provision contained therein for a subsequent adjustment of such number) issuable upon the exercise of such Options or the conversion or exchange of such Convertible Securities, or in the case of Options for Convertible Securities, the exercise of such Options for Convertible Securities and the conversion or exchange of such Convertible Securities.

4.4.6 Multiple Closing Dates. In the event the Corporation shall issue on more than one date Additional Shares of Common Stock that are a part of one transaction or a series of related transactions and that would result in an adjustment to the Series A Conversion Price, Series A-1 Conversion Price, Series B Conversion Price, Series C Conversion Price or Series D Conversion Price pursuant to the terms of Subsection 4.4.4 above then, upon the final such issuance, the Series A Conversion Price, Series A-1 Conversion Price, Series B Conversion Price, Series C Conversion Price or Series D Conversion Price, as the case may be, shall be readjusted to give effect to all such issuances as if they occurred on the date of the first such issuance (and without giving effect to any additional adjustments as a result of any such subsequent issuances within such period).

4.5 Adjustment for Stock Splits and Combinations. If the Corporation shall at any time or from time to time after the Series D Original Issue Date effect a subdivision of the outstanding Common Stock, the Series A Conversion Price, Series A-1 Conversion Price, Series B Conversion Price, Series C Conversion Price and Series D Conversion Price in effect immediately before that subdivision shall be proportionately decreased so that the number of shares of Common Stock issuable on conversion of each share of such series shall be increased in proportion to such increase in the aggregate number of shares of Common Stock outstanding. If the Corporation shall at any time or from time to time after the Series D Original Issue Date combine the outstanding shares of Common Stock, the Series A Conversion Price, Series A-1 Conversion Price, Series B Conversion Price, Series C Conversion Price and Series D Conversion Price in effect immediately before the combination shall be proportionately increased so that the number of shares of Common Stock issuable on conversion of each share of such series shall be decreased in proportion to such decrease in the aggregate number of shares of Common Stock outstanding. Any adjustment under this subsection shall become effective at the close of business on the date the subdivision or combination becomes effective.

4.6 Adjustment for Certain Dividends and Distributions. In the event the Corporation at any time or from time to time after the Series D Original Issue Date shall make or issue, or fix a record date for the determination of holders of Common Stock entitled to receive, a dividend or other distribution payable on the Common Stock in additional shares of Common

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Stock, then and in each such event the Series A Conversion Price, Series A-1 Conversion Price, Series B Conversion Price, Series C Conversion Price and Series D Conversion Price in effect immediately before such event shall be decreased as of the time of such issuance or, in the event such a record date shall have been fixed, as of the close of business on such record date, by multiplying the Series A Conversion Price, Series A-1 Conversion Price, Series B Conversion Price, Series C Conversion Price or Series D Conversion Price, as applicable, then in effect by a fraction:

- (1) the numerator of which shall be the total number of shares of Common Stock issued and outstanding immediately prior to the time of such issuance or the close of business on such record date, and
- (2) the denominator of which shall be the total number of shares of Common Stock issued and outstanding immediately prior to the time of such issuance or the close of business on such record date plus the number of shares of Common Stock issuable in payment of such dividend or distribution.

Notwithstanding the foregoing, (a) if such record date shall have been fixed and such dividend is not fully paid or if such distribution is not fully made on the date fixed therefor, the Series A Conversion Price, Series A-1 Conversion Price, Series B Conversion Price, Series C Conversion Price and Series D Conversion Price shall be recomputed accordingly as of the close of business on such record date and thereafter the Series A Conversion Price, Series A-1 Conversion Price, Series B Conversion Price, Series C Conversion Price and Series D Conversion Price shall be adjusted pursuant to this subsection as of the time of actual payment of such dividends or distributions; and (b) no such adjustment shall be made if the holders of Designated Preferred Stock simultaneously receive a dividend or other distribution of shares of Common Stock in a number equal to the number of shares of Common Stock as they would have received if all outstanding shares of Designated Preferred Stock had been converted into Common Stock on the date of such event.

4.7 Adjustments for Other Dividends and Distributions. In the event the Corporation at any time or from time to time after the Series D Original Issue Date shall make or issue, or fix a record date for the determination of holders of Common Stock entitled to receive, a dividend or other distribution payable in securities of the Corporation (other than a distribution of shares of Common Stock in respect of outstanding shares of Common Stock) or in other property and the provisions of Section 1 do not apply to such dividend or distribution, then and in each such event the holders of Designated Preferred Stock shall receive, simultaneously with the distribution to the holders of Common Stock, a dividend or other distribution of such securities or other property in an amount equal to the amount of such securities or other property as they would have received if all outstanding shares of Designated Stock had been converted into Common Stock on the date of such event.

4.8 Adjustment for Merger or Reorganization, etc. Subject to the provisions of Subsection 2.3, if there shall occur any reorganization, recapitalization, reclassification,

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consolidation or merger involving the Corporation in which the Common Stock (but not the Designated Preferred Stock) is converted into or exchanged for securities, cash or other property (other than a transaction covered by Subsections 4.4, 4.6 or 4.7), then, following any such reorganization, recapitalization, reclassification, consolidation or merger, each share of Designated Preferred Stock shall thereafter be convertible in lieu of the Common Stock into which it was convertible prior to such event into the kind and amount of securities, cash or other property which a holder of the number of shares of Common Stock of the Corporation issuable upon conversion of one share of such series of Designated Preferred Stock immediately prior to such reorganization, recapitalization, reclassification, consolidation or merger would have been entitled to receive pursuant to such transaction; and, in such case, appropriate adjustment (as determined in good faith by the Board of Directors) shall be made in the application of the provisions in this Section 4 with respect to the rights and interests thereafter of the holders of the Designated Preferred Stock, to the end that the provisions set forth in this Section 4 (including provisions with respect to changes in and other adjustments of the Series A Conversion Price, Series A-1 Conversion Price, Series B Conversion Price, Series C Conversion Price or Series D Conversion Price) shall thereafter be applicable, as nearly as reasonably may be, in relation to any securities or other property thereafter deliverable upon the conversion of the Designated Preferred Stock.

4.9 Certificate as to Adjustments. Upon the occurrence of each adjustment or readjustment of the Series A Conversion Price, Series A-1 Conversion Price, Series B Conversion Price, Series C Conversion Price or Series D Conversion Price pursuant to this Section 4, the Corporation at its expense shall, as promptly as reasonably practicable but in any event not later than ten (10) calendar days thereafter, compute such adjustment or readjustment in accordance with the terms hereof and furnish to each holder of Designated Preferred Stock a certificate setting forth such adjustment or readjustment (including the kind and amount of securities, cash or other property into which the Designated Preferred Stock is convertible) and showing in detail the facts upon which such adjustment or readjustment is based. The Corporation shall, as promptly as reasonably practicable after the written request at any time of any holder of Designated Preferred Stock (but in any event not later than ten (10) calendar days thereafter), furnish or cause to be furnished to such holder a certificate setting forth (i) the Series A Conversion Price, the Series A-1 Conversion Price, Series B Conversion Price, Series C Conversion Price and Series D Conversion Price then in effect, and (ii) the number of shares of Common Stock and the amount, if any, of other securities, cash or property which then would be received upon the conversion of Designated Preferred Stock.

4.10 Notice of Record Date. In the event:

(a) the Corporation shall take a record of the holders of its Common Stock (or other capital stock or securities at the time issuable upon conversion of the Designated Preferred Stock) for the purpose of entitling or enabling them to receive any dividend or other distribution, or to receive any right to subscribe for or purchase any shares of capital stock of any class or any other securities, or to receive any other security; or

(b) of any capital reorganization of the Corporation, any reclassification of the Common Stock of the Corporation, or any Deemed Liquidation Event; or

(c) of the voluntary or involuntary dissolution, liquidation or winding-up of the Corporation,

then, and in each such case, the Corporation will send or cause to be sent to the holders of the Designated Preferred Stock a notice specifying, as the case may be, (i) the record date for such dividend, distribution or right, and the amount and character of such dividend, distribution or right, or (ii) the effective date on which such reorganization, reclassification, consolidation, merger, transfer, dissolution, liquidation or winding-up is proposed to take place, and the time, if any is to be fixed, as of which the holders of record of Common Stock (or such other capital stock or securities at the time issuable upon the conversion of the Designated Preferred Stock) shall be entitled to exchange their shares of Common Stock (or such other capital stock or securities) for securities or other property deliverable upon such reorganization, reclassification, consolidation, merger, transfer, dissolution, liquidation or winding-up, and the amount per share and character of such exchange applicable to the Designated Preferred Stock and the Common Stock. Such notice shall be sent at least 10 days prior to the record date or effective date for the event specified in such notice.

5. Mandatory Conversion.

5.1 Trigger Events.

5.1.1 Upon the closing of the sale of shares of Common Stock to the public at a price of at least \$1.77 per share (subject to appropriate adjustment in the event of any stock dividend, stock split, combination or other similar recapitalization affecting such shares), in a firm-commitment underwritten public offering pursuant to an effective registration statement under the Securities Act of 1933, as amended, resulting in at least \$40,000,000 of gross proceeds to the Corporation (the "**Qualified IPO**"), all outstanding shares of Designated Preferred Stock shall automatically be converted into shares of Common Stock, at the then effective conversion rate for the applicable series.

5.1.2 Upon the date and time, or the occurrence of an event, specified by vote or written consent of the holders of outstanding shares of Designated Preferred Stock representing at least eighty percent (80%) of the then outstanding shares of Designated Preferred Stock, voting together as a single class on an as converted to Common Stock basis, all outstanding shares of Designated Preferred Stock shall automatically be converted into shares of Common Stock, at the then effective conversion rate for the for the applicable series.

5.1.3 The time of the closing described in Subsection 5.1.1 or the date and time specified or the time of the event specified in the vote or written consent described in Subsection 5.1.2 is referred to herein as the "**Mandatory Conversion Time**" for the shares of Designated Preferred Stock to be mandatorily converted as described in such subsections.

5.2 Procedural Requirements. All holders of record of shares of Designated Preferred Stock to be converted under Subsection 5.1 shall be sent written notice of the applicable Mandatory Conversion Time and the place designated for mandatory conversion of all such shares of Designated Preferred Stock pursuant to this Section 5. Such notice need not be sent in advance of the occurrence of such Mandatory Conversion Time. Upon receipt of such

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notice, each such holder of shares of Designated Preferred Stock shall surrender his, her or its certificate or certificates for all such shares (or, if such holder alleges that such certificate has been lost, stolen or destroyed, a lost certificate affidavit and agreement reasonably acceptable to the Corporation to indemnify the Corporation against any claim that may be made against the Corporation on account of the alleged loss, theft or destruction of such certificate) to the Corporation at the place designated in such notice, and shall thereafter receive certificates for the number of shares of Common Stock to which such holder is entitled pursuant to this Section 5. At the applicable Mandatory Conversion Time, all outstanding shares of Designated Preferred Stock to be converted shall be deemed to have been converted into shares of Common Stock, which shall be deemed to be outstanding of record, and all rights with respect to the Designated Preferred Stock so converted, including the rights, if any, to receive notices and vote (other than as a holder of Common Stock), will terminate, except only the rights of the holders thereof, upon surrender of their certificate or certificates (or lost certificate affidavit and agreement) therefor, to receive the items provided for in the last sentence of this Subsection 5.2. If so required by the Corporation, certificates surrendered for conversion shall be endorsed or accompanied by written instrument or instruments of transfer, in form satisfactory to the Corporation, duly executed by the registered holder or by his, her or its attorney duly authorized in writing. As soon as practicable after the applicable Mandatory Conversion Time and the surrender of the certificate or certificates (or lost certificate affidavit and agreement) for Designated Preferred Stock converted at such Mandatory Conversion Time, the Corporation shall issue and deliver to such holder, or to his, her or its nominees, a certificate or certificates for the number of full shares of Common Stock issuable on such conversion in accordance with the provisions hereof, together with cash as provided in Subsection 4.2 in lieu of any fraction of a share of Common Stock otherwise issuable upon such conversion and the payment of any declared but unpaid dividends (but not any undeclared Accruing Dividends) on the shares of Designated Preferred Stock converted.

5.3 Effect of Mandatory Conversion. All shares of Designated Preferred Stock to be converted under Subsection 5.1 shall, from and after the applicable Mandatory Conversion Time, no longer be deemed to be outstanding and, notwithstanding the failure of the holder or holders thereof to surrender the certificates for such shares on or prior to such time, all rights with respect to such shares shall immediately cease and terminate at such Mandatory Conversion Time, except only the right of the holders thereof to receive shares of Common Stock in exchange therefor and to receive payment of any dividends declared but unpaid thereon (but not any Accruing Dividends). Such converted Designated Preferred Stock shall be retired and cancelled and may not be reissued, and the Corporation may thereafter take such appropriate action (without the need for stockholder action) as may be necessary to reduce the authorized number of shares of Designated Preferred Stock accordingly.

#### 5A. Special Mandatory Conversion.

5A.1. Trigger Events. In the event that any holder of shares of Series D Preferred Stock fails to purchase all of the shares of Series D Preferred Stock that such holder is contractually obligated or required to purchase pursuant to the Series D Purchase Agreement at either the Second Tranche Closing (as defined in the Series D Purchase Agreement) or the Third Tranche Closing (as defined in the Series D Purchase Agreement), then, effective upon, subject to, and concurrently with, the consummation in accordance with the Series D Purchase

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Agreement of the Second Tranche Closing or the Third Tranche Closing, as the case may be, (i) each share of Series D Preferred Stock held by such holder immediately prior to the Second Tranche Closing or the Third Tranche Closing, as the case may be, shall automatically, and without any further action on the part of such holder, be converted into shares of Common Stock at the rate of one (1) share of Common Stock for every ten (10) shares of Series D Preferred Stock owned or held by such holder immediately prior to the Second Tranche Closing or the Third Tranche Closing, as the case may be. For purposes of determining the applicability of this Subsection 5A.1 to a holder of Series D Preferred Stock that is contractually obligated or required to purchase shares of Series D Preferred Stock pursuant to the Series D Purchase Agreement at the Second Tranche Closing or the Third Tranche Closing, as the case may be, such holder shall be entitled to aggregate the number of shares of Series D Preferred Stock purchased pursuant to the Series D Purchase Agreement at the Second Tranche Closing or the Third Tranche Closing, as the case may be, by an Affiliate of such holder together with such holder's own purchases pursuant to the Series D Purchase Agreement at the Second Tranche Closing or the Third Tranche Closing, as the case may be (provided that no shares of Series D Preferred Stock purchased pursuant to the Series D Purchase Agreement at the Second Tranche Closing or the Third Tranche Closing, as the case may be, by any group of entities or persons affiliated with a holder of Series D Preferred Stock that is contractually obligated or required to purchase shares of Series D Preferred Stock pursuant to the Series D Purchase Agreement at the Second Tranche Closing or the Third Tranche Closing, as the case may be, may be attributed to more than one such holder of Series D Preferred Stock so contractually obligated or required). Any automatic conversion pursuant to this Subsection 5A.1 is referred to as a "**Special Mandatory Conversion**."

5A.2. Procedural Requirements. Upon a Special Mandatory Conversion, each holder of shares of Series D Preferred Stock converted pursuant to Subsection 5A.1 shall be sent written notice of such Special Mandatory Conversion and the place designated for mandatory conversion of all such shares of Series D Preferred Stock pursuant to this Subsection 5A; provided, however, that any failure or delay in delivering such notice shall not affect the mandatory and automatic conversion of such shares pursuant to Subsection 5A.1. Upon receipt of such notice, each holder of such shares of Series D Preferred Stock in certificated form shall surrender his, her or its certificate or certificates for all such shares (or, if such holder alleges that any such certificate has been lost, stolen or destroyed, a lost certificate affidavit and agreement reasonably acceptable to the Corporation to indemnify the Corporation against any claim that may be made against the Corporation on account of the alleged loss, theft or destruction of such certificate) to the Corporation at the place designated in such notice. If so required by the Corporation, any certificates surrendered for conversion shall be endorsed or accompanied by written instrument or instruments of transfer, in form satisfactory to the Corporation, duly executed by the registered holder or by his, her or its attorney duly authorized in writing. All rights with respect to the Series D Preferred Stock converted pursuant to Subsection 5A.1, including the rights, if any, to receive notices and vote (other than as a holder of Common Stock), will terminate at the time of the Special Mandatory Conversion (notwithstanding the failure of the holder or holders thereof to surrender any certificates for such shares at or prior to such time), except only the rights of the holders thereof, upon surrender of any certificate or certificates of such holders therefor (or lost certificate affidavit and agreement), to receive the items provided for in the next sentence of this Subsection 5A.2. As soon as practicable after the Special Mandatory Conversion and, if applicable, the surrender of any certificate or certificates

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(or lost certificate affidavit and agreement) for Series D Preferred Stock so converted, the Corporation shall (a) issue and deliver to such holder, or to his, her or its nominees, a certificate or certificates for the number of full shares of Common Stock issuable on such conversion in accordance with the provisions hereof and (b) pay cash as provided in Subsection 4.2 in lieu of any fraction of a share of Common Stock otherwise issuable upon such conversion and the payment of any declared but unpaid dividends on the shares of Series D Preferred Stock converted (but not any undeclared Accruing Dividends). Such converted Series D Preferred Stock shall be retired and cancelled and may not be reissued as shares of such series, and the Corporation may thereafter take such appropriate action (without the need for stockholder action) as may be necessary to reduce the authorized number of shares of Series D Preferred Stock accordingly.

## 6. Redemption.

6.1 Redemption. Shares of Designated Preferred Stock shall be redeemed by the Corporation out of funds legally available therefor at a price per share equal to (i) in the case of the Series A Preferred Stock, the Series A Original Issue Price, plus any Accruing Dividends accrued but unpaid thereon, whether or not declared, together with any other dividends declared but unpaid thereon (the “**Series A Redemption Price**”), (ii) in the case of the Series A-1 Preferred Stock, the Series A-1 Original Issue Price, plus any Accruing Dividends accrued but unpaid thereon, whether or not declared, together with any other dividends declared but unpaid thereon (the “**Series A-1 Redemption Price**”), (iii) in the case of the Series B Preferred Stock, the Series B Original Issue Price, plus any Accruing Dividends accrued but unpaid thereon, whether or not declared, together with any other dividends declared but unpaid thereon (the “**Series B Redemption Price**”), (iv) in the case of the Series C Preferred Stock, the Series C Original Issue Price, plus any Accruing Dividends accrued but unpaid thereon, whether or not declared, together with any other dividends declared but unpaid thereon (the “**Series C Redemption Price**”), and (v) in the case of the Series D Preferred Stock, the Series D Original Issue Price, plus any Accruing Dividends accrued but unpaid thereon, whether or not declared, together with any other dividends declared but unpaid thereon (the “**Series D Redemption Price**”), in three annual installments commencing 60 days after receipt by the Corporation at any time on or after the fifth anniversary of the Series D Original Issue Date, from the holders of outstanding shares of Designated Preferred Stock representing at least eighty percent (80%) of the then outstanding shares of Designated Preferred Stock, on an as converted to Common Stock basis, of written notice requesting redemption of all shares of Designated Preferred Stock (the date of each such installment being referred to as a “**Redemption Date**”). On each Redemption Date, the Corporation shall redeem, on a pro rata basis in accordance with the number of shares of Series A Preferred Stock, Series A-1 Preferred Stock, Series B Preferred Stock, Series C Preferred Stock, and Series D Preferred Stock, owned by each holder, that number of outstanding shares of Series A Preferred Stock, Series A-1 Preferred Stock, Series B Preferred Stock, Series C Preferred Stock, and Series D Preferred Stock, determined by dividing (i) in the case of the Series A Preferred Stock, (A) the total number of shares of Series A Preferred Stock outstanding immediately prior to such Redemption Date by (B) the number of remaining Redemption Dates (including the Redemption Date to which such calculation applies), (ii) in the case of the Series A-1 Preferred Stock, (A) the total number of shares of Series A-1 Preferred Stock outstanding immediately prior to such Redemption Date by (B) the number of remaining Redemption Dates (including the Redemption Date to which such calculation applies), (iii) in the case of the Series

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B Preferred Stock, (A) the total number of shares of Series B Preferred Stock outstanding immediately prior to such Redemption Date by (B) the number of remaining Redemption Dates (including the Redemption Date to which such calculation applies), (iv) in the case of the Series C Preferred Stock, (A) the total number of shares of Series C Preferred Stock outstanding immediately prior to such Redemption Date by (B) the number of remaining Redemption Dates (including the Redemption Date to which such calculation applies), and (v) in the case of the Series D Preferred Stock, (A) the total number of shares of Series D Preferred Stock outstanding immediately prior to such Redemption Date by (B) the number of remaining Redemption Dates (including the Redemption Date to which such calculation applies). If the Corporation does not have sufficient funds legally available to redeem on any Redemption Date all shares of Designated Preferred Stock to be redeemed on such Redemption Date, then the Corporation shall redeem first, a pro rata portion of each holder’s redeemable shares of Series D Preferred Stock (in accordance with the relative priorities or preferences of the Series D Preferred Stock and any such Other Preferred Stock), to the fullest extent of the funds legally available therefor, based on the respective amounts which would otherwise be payable in respect of the shares of Series D Preferred to be redeemed if the funds legally available therefor were sufficient to redeem all such shares, and shall redeem the remaining shares of Series D Preferred Stock to have been redeemed as soon as practicable after the Corporation has funds legally available therefor, until all shares of Series D Preferred Stock to have been redeemed as of such Redemption Date shall have been redeemed in full, second, a pro rata portion of each holder’s redeemable shares of Series C Preferred Stock out of funds legally available therefor, based on the respective amounts which would otherwise be payable in respect of the shares to be redeemed if the legally available funds were sufficient to redeem all such shares, and shall redeem the remaining shares of Series C Preferred Stock to have been redeemed as soon as practicable after the Corporation has funds legally available therefor, third, a pro rata portion of each holder’s redeemable shares of Series B Preferred Stock out of funds legally available therefor, based on the respective amounts which would otherwise be payable in respect of the shares to be redeemed if the legally available funds were sufficient to redeem all such shares, and shall redeem the remaining shares of Series B Preferred Stock to have been redeemed as soon as practicable after the Corporation has funds legally available therefor, and then, a pro rata portion of each holder’s redeemable shares of Series A Preferred Stock and Series A-1 Preferred Stock out of funds legally available therefor, based on the respective amounts which would otherwise be payable in respect of the shares to be redeemed if the legally available funds were sufficient to redeem all such shares, and shall redeem the remaining shares of Series A Preferred Stock and Series A-1 Preferred Stock to have been redeemed as soon as practicable after the Corporation has funds legally available therefor.

6.2 Redemption Notice. Written notice of the mandatory redemption (the “**Redemption Notice**”) shall be sent to each holder of record of Designated Preferred Stock not less than forty (40) calendar days prior to each Redemption Date. Each Redemption Notice shall state:

(a) the number of shares of Series A Preferred Stock, Series A-1 Preferred Stock, Series B Preferred Stock, Series C Preferred Stock, and Series D Preferred Stock held by the holder that the Corporation shall redeem on the Redemption Date specified in the Redemption Notice;

(b) the Redemption Date and the applicable Series A Redemption Price, Series A-1 Redemption Price, Series B Redemption Price, Series C Redemption Price, and Series D Redemption Price;

(c) the date upon which the holder’s right to convert such shares terminates (as determined in accordance with Subsection 4.1); and

(d) that the holder is to surrender to the Corporation, in the manner and at the place designated, his, her or its certificate or certificates representing the shares of Designated Preferred Stock to be redeemed.

6.3 Surrender of Certificates; Payment. On or before the applicable Redemption Date, each holder of shares of Designated Preferred Stock to be redeemed on such Redemption Date, unless such holder has exercised his, her or its right to convert such shares as provided in Section 4, shall surrender the certificate or certificates representing such shares (or, if such registered holder alleges that such certificate has been lost, stolen or destroyed, a lost certificate affidavit and agreement reasonably acceptable to the Corporation to indemnify the Corporation against any claim that may be made against the Corporation on account of the alleged loss, theft or destruction of such certificate) to the Corporation, in the manner and at the place designated in the Redemption Notice, and thereupon the Series A Redemption Price, Series A-1 Redemption Price, Series B Redemption Price, Series C Redemption Price, or Series D Redemption Price, as the case may be, for such shares shall be payable to the order of the person whose name appears on such certificate or certificates as the owner thereof. In the event less than all of the shares of Designated Preferred Stock represented by a certificate are redeemed, a new certificate representing the unredeemed shares of Designated Preferred Stock shall promptly be issued to such holder.

6.4 Rights Subsequent to Redemption. If the Redemption Notice shall have been duly given, and if on the applicable Redemption Date the aggregate Series A Redemption Price, Series A-1 Redemption Price, Series B Redemption Price, Series C Redemption Price and Series D Redemption Price payable

upon redemption of the shares of Designated Preferred Stock to be redeemed on such Redemption Date is paid or tendered for payment or deposited with an independent payment agent so as to be available therefor, then notwithstanding that the certificates evidencing any of the shares of Designated Preferred Stock so called for redemption shall not have been surrendered, dividends with respect to such shares of Designated Preferred Stock shall cease to accrue after such Redemption Date and all rights with respect to such shares shall forthwith after the Redemption Date terminate, except only the right of the holders to receive the Series A Redemption Price, Series A-1 Redemption Price, Series B Redemption Price, Series C Redemption Price, or Series D Redemption Price therefor without interest upon surrender of their certificate or certificates therefor.

7. **Redeemed or Otherwise Acquired Shares.** Any shares of Designated Preferred Stock which are redeemed or otherwise acquired by the Corporation or any of its subsidiaries shall be automatically and immediately cancelled and retired and shall not be reissued, sold or transferred. Neither the Corporation nor any of its subsidiaries may exercise any voting or other rights granted to the holders of Designated Preferred Stock following redemption thereof.

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8. **Waiver.** Any of the rights, powers, preferences and other terms of the Designated Preferred Stock set forth herein may be waived on behalf of all holders of Designated Preferred Stock by the affirmative written consent or vote of the holders of at least eighty percent (80%) of the shares of Designated Preferred Stock then outstanding (voting together as a single class on an as converted to Common Stock basis and not as separate series).

9. **Notice.** Any notice required or permitted by the provisions of this Article Fourth to be given to a holder of shares of Designated Preferred Stock shall be mailed, postage prepaid, to the post office address last shown on the records of the Corporation, or given by electronic communication in compliance with the provisions of the General Corporation Law, and shall be deemed sent upon such mailing or electronic transmission.

**FIFTH:** Subject to any additional vote required by the Certificate of Incorporation, in furtherance and not in limitation of the powers conferred by statute, the Board of Directors is expressly authorized to make, repeal, alter, amend and rescind any or all of the Bylaws of the Corporation.

**SIXTH:** Subject to any additional vote required by the Certificate of Incorporation, the number of directors of the Corporation shall be determined in the manner set forth in the Bylaws of the Corporation.

**SEVENTH:** Elections of directors need not be by written ballot unless the Bylaws of the Corporation shall so provide.

**EIGHTH:** Meetings of stockholders may be held within or without the State of Delaware, as the Bylaws of the Corporation may provide. The books of the Corporation may be kept outside the State of Delaware at such place or places as may be designated from time to time by the Board of Directors or in the Bylaws of the Corporation.

**NINTH:** To the fullest extent permitted by law, a director of the Corporation shall not be personally liable to the Corporation or its stockholders for monetary damages for breach of fiduciary duty as a director. If the General Corporation Law or any other law of the State of Delaware is amended after approval by the stockholders of this Article Ninth to authorize corporate action further eliminating or limiting the personal liability of directors, then the liability of a director of the Corporation shall be eliminated or limited to the fullest extent permitted by the General Corporation Law as so amended.

Any repeal or modification of the foregoing provisions of this Article Ninth by the stockholders of the Corporation shall not adversely affect any right or protection of a director of the Corporation existing at the time of, or increase the liability of any director of the Corporation with respect to any acts or omissions of such director occurring prior to, such repeal or modification.

**TENTH:** To the fullest extent permitted by applicable law, the Corporation is authorized to provide indemnification of (and advancement of expenses to) directors, officers and agents of the Corporation (and any other persons to which the General Corporation Law permits the Corporation to provide indemnification) through Bylaw provisions, agreements with such agents

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or other persons, vote of stockholders or disinterested directors or otherwise, in excess of the indemnification and advancement otherwise permitted by Section 145 of the General Corporation Law.

Any amendment, repeal or modification of the foregoing provisions of this Article Tenth shall not adversely affect any right or protection of any director, officer or other agent of the Corporation existing at the time of such amendment, repeal or modification.

**ELEVENTH:** The Corporation renounces any interest or expectancy of the Corporation in, or in being offered an opportunity to participate in, any Excluded Opportunity. An “**Excluded Opportunity**” is any matter, transaction or interest that is presented to, or acquired, created or developed by, or which otherwise comes into the possession of, (i) any director of the Corporation who is not an employee of the Corporation or any of its subsidiaries, or (ii) any holder of Designated Preferred Stock or any partner, member, director, stockholder, employee or agent of any such holder, other than someone who is an employee of the Corporation or any of its subsidiaries (collectively, “**Covered Persons**”), unless such matter, transaction or interest is presented to, or acquired, created or developed by, or otherwise comes into the possession of, a Covered Person expressly and solely in such Covered Person’s capacity as a director of the Corporation.

\* \* \*

4. That the foregoing amendment and restatement was approved by the holders of the requisite number of shares of this corporation in accordance with Section 228 of the General Corporation Law.

5. That this Fifth Amended and Restated Certificate of Incorporation, which restates and integrates and further amends the provisions of this corporation’s Prior Charter, has been duly adopted in accordance with Sections 242 and 245 of the General Corporation Law.

*[The remainder of the page has intentionally been left blank.]*

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**IN WITNESS WHEREOF,** this Fifth Amended and Restated Certificate of Incorporation has been executed by a duly authorized officer of this corporation on this 9th day of May, 2014.

By: /s/ Timothy Noyes  
Timothy Noyes  
President and Chief Executive Officer

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**[Signature Page to 5th A&R Charter]**

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**BYLAWS**  
**OF**  
**PROTEON THERAPEUTICS, INC.**  
**(A DELAWARE CORPORATION)**

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**BYLAWS**  
**OF**  
**PROTEON THERAPEUTICS, INC.**  
**(A DELAWARE CORPORATION)**

**ARTICLE I**  
**OFFICES**

**Section 1. Registered Office.** The registered office of the corporation in the State of Delaware shall be in the City of Wilmington, County of New Castle.

**Section 2. Other Offices.** The corporation shall also have and maintain an office or principal place of business at such place as may be fixed by the Board of Directors, and may also have offices at such other places, both within and without the State of Delaware, as the Board of Directors may from time to time determine or the business of the corporation may require.

**ARTICLE II**  
**CORPORATE SEAL**

**Section 3. Corporate Seal.** The Board of Directors may adopt a corporate seal. The corporate seal shall consist of a die bearing the name of the corporation and the inscription, "Corporate Seal-Delaware." Said seal may be used by causing it or a facsimile thereof to be impressed or affixed or reproduced or otherwise.

**ARTICLE III**  
**STOCKHOLDERS' MEETINGS**

**Section 4. Place of Meetings.** Meetings of the stockholders of the corporation may be held at such place, either within or without the State of Delaware, as may be determined from time to time by the Board of Directors. The Board of Directors may, in its sole discretion, determine that the meeting shall not be held at any place, but may instead be held solely by means of remote communication as authorized by Section 211(a)(2) of the Delaware General Corporation Law ("**DGCL**"). If so authorized, and subject to such guidelines and procedures as the board of directors may adopt, stockholders and proxyholders not physically present at a meeting of stockholders may, by means of remote communication, participate in a meeting of stockholders whether such meeting is to be held at a designated place or solely by means of remote communication, provided that (i) the corporation shall implement reasonable measures to verify that each person deemed present and permitted to vote at the meeting by means of remote communication is a stockholder or proxyholder, (ii) the corporation shall implement reasonable measures to provide such stockholders and proxyholders a reasonable opportunity to participate

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in the meeting and to vote on matters submitted to the stockholders, including an opportunity to read or hear the proceedings of the meeting substantially concurrently with such proceedings, and (iii) if any stockholder or proxyholder votes or takes other action at the meeting by means of remote communication, a record of such vote or other action shall be maintained by the corporation. Any adjourned session of any meeting shall be held at the place designated in the vote of adjournment.

**Section 5. Annual Meeting.**

(a) The annual meeting of the stockholders of the corporation, for the purpose of election of directors and for such other business as may lawfully come before it, shall be held on such date and at such time as may be designated from time to time by the Board of Directors. Nominations of persons for election to the Board of Directors of the corporation and the proposal of business to be considered by the stockholders may be made at an annual meeting of stockholders: (i) pursuant to the corporation's notice of meeting of stockholders; (ii) by or at the direction of the Board of Directors; or (iii) by any stockholder of the corporation who was a stockholder of record at the time of giving of notice provided for in the following paragraph, who is entitled to vote at the meeting and who complied with the notice procedures set forth in Section 5.

(b) At an annual meeting of the stockholders, only such business shall be conducted as shall have been properly brought before the meeting. For nominations or other business to be properly brought before an annual meeting by a stockholder pursuant to clause (iii) of Section 5(a) of these Bylaws, (i) the stockholder must have given timely notice thereof in writing to the Secretary of the corporation, and (ii) such other business must be a proper matter for stockholder action under the DGCL. Such stockholder's notice shall set forth, as to any other business that the stockholder proposes to bring before the meeting, a brief description of the business desired to be brought before the meeting, the reasons for conducting such business at the meeting and any material interest in such business of such stockholder and the beneficial owner, if any, on whose behalf the proposal is made. Such stockholder's notice shall be timely if delivered to the Secretary at the principal executive offices of the Corporation not later than the close of business on the tenth (10<sup>th</sup>) day nor earlier than the close of business on the sixtieth (60<sup>th</sup>) day prior to the date of the annual meeting.

(c) Only such business shall be conducted at a meeting of stockholders as shall have been brought before the meeting in accordance with the procedures set forth in this Section 5. Except as otherwise provided by law, the Chairman of the meeting shall have the power and duty to determine whether a nomination or any business proposed to be brought before the meeting was made, or proposed, as the case may be, in accordance with the procedures set forth in these Bylaws and, if any proposed nomination or business is not in compliance with these Bylaws, to declare that such defective proposal or nomination shall not be presented for stockholder action at the meeting and shall be disregarded.

(d) If the election for directors shall not be held on the day designated by these by-laws, the directors shall cause the election to be held as soon thereafter as convenient, and to that end, if the annual meeting is omitted on the day herein provided therefor or if the election of directors shall not be held thereat, a special meeting of the stockholders may be held

in place of such omitted meeting or election, and any business transacted or election held at such special meeting shall have the same effect as if transacted or held at the annual meeting, and in such case all references in these by-laws to the annual meeting of the stockholders, or to the annual election of directors, shall be deemed to refer to or include such special meeting. Any such special meeting shall be called and the purposes thereof shall be specified in the call, as provided in Section 6.

#### **Section 6. Special Meetings.**

(a) Special meetings of the stockholders of the corporation may be called, for any purpose or purposes, by (i) the Chairman of the Board of Directors, (ii) the Chief Executive Officer, or (iii) the Board of Directors pursuant to a resolution adopted by a majority of the total number of authorized directors (whether or not there exist any vacancies in previously authorized directorships at the time any such resolution is presented to the Board of Directors for adoption) or (iv) by the holders of shares entitled to cast not less than ten percent (10%) of the votes at the meeting, and shall be held at such place, on such date, and at such time as the Board of Directors shall fix. At any time or times that the corporation is subject to Section 2115(b) of the California General Corporation Law ("CGCL"), stockholders holding five percent (5%) or more of the outstanding shares shall have the right to call a special meeting of stockholders as set forth in Section 18(b) herein.

(b) If a special meeting is properly called by any person or persons other than the Board of Directors, the request shall be in writing, specifying the general nature of the business proposed to be transacted, and shall be delivered personally or sent by certified or registered mail, return receipt requested, or by telegraphic or other facsimile transmission to the Chairman of the Board of Directors, the Chief Executive Officer, or the Secretary of the corporation. No business may be transacted at such special meeting otherwise than specified in such notice. The Board of Directors shall determine the time and place of such special meeting, which shall be held not less than thirty-five (35) nor more than one hundred twenty (120) days after the date of the receipt of the request. Upon determination of the time and place of the meeting, the officer receiving the request shall cause notice to be given to the stockholders entitled to vote, in accordance with the provisions of Section 7 of these Bylaws. Nothing contained in this paragraph (b) shall be construed as limiting, fixing, or affecting the time when a meeting of stockholders called by action of the Board of Directors may be held.

**Section 7. Notice of Meetings.** Except as otherwise provided by law, notice, given in writing or by electronic transmission, of each meeting of stockholders shall be given not less than ten (10) nor more than sixty (60) days before the date of the meeting to each stockholder entitled to vote at such meeting, such notice to specify the place, if any, date and hour, in the case of special meetings, the purpose or purposes of the meeting, and the means of remote communications, if

any, by which stockholders and proxyholders may be deemed to be present in person and vote at any such meeting. If mailed, notice is given when deposited in the United States mail, postage prepaid, directed to the stockholder at such stockholder's address as it appears on the records of the corporation. Notice of the time, place, if any, and purpose of any meeting of stockholders may be waived in writing, signed by the person entitled to notice thereof or by electronic transmission by such person, either before or after such meeting, and will be waived by any stockholder by his attendance thereat in person, by remote communication, if applicable, or by proxy, except when the stockholder attends a meeting for the express purpose of objecting, at the beginning of the meeting, to the transaction of any business because the meeting is not lawfully called or convened. Any stockholder so waiving notice of such meeting shall be bound by the proceedings of any such meeting in all respects as if due notice thereof had been given.

**Section 8. Quorum.** At all meetings of stockholders, except where otherwise provided by statute or by the Certificate of Incorporation, or by these Bylaws, the presence, in person, by remote communication, if applicable, or by proxy duly authorized, of the holders of a majority of the outstanding shares of stock entitled to vote shall constitute a quorum for the transaction of business. In the absence of a quorum, any meeting of stockholders may be adjourned, from time to time, either by the chairman of the meeting or by vote of the holders of a majority of the shares represented thereat, but no other business shall be transacted at such meeting. The stockholders present at a duly called or convened meeting, at which a quorum is present, may continue to transact business until adjournment, notwithstanding the withdrawal of enough stockholders to leave less than a quorum. Except as otherwise provided by statute, or by the Certificate of Incorporation or these Bylaws, in all matters other than the election of directors, the affirmative vote of a majority of shares present in person, by remote communication, if applicable, or represented by proxy duly authorized at the meeting and entitled to vote generally on the subject matter shall be the act of the stockholders. Except as otherwise provided by statute, the Certificate of Incorporation or these Bylaws, directors shall be elected by a plurality of the votes of the shares present in person, by remote communication, if applicable, or represented by proxy duly authorized at the meeting and entitled to vote generally on the election of directors. Where a separate vote by a class or classes or series is required, except where otherwise provided by the statute or by the Certificate of Incorporation or these Bylaws, a majority of the outstanding shares of such class or classes or series, present in person, by remote communication, if applicable, or represented by proxy duly authorized, shall constitute a quorum entitled to take action with respect to that vote on that matter. Except where otherwise provided by statute or by the Certificate of Incorporation or these Bylaws, the affirmative vote of the majority (plurality, in the case of the election of directors) of shares of such class or classes or series present in person, by remote communication, if applicable, or represented by proxy at the meeting shall be the act of such class or classes or series.

**Section 9. Adjournment and Notice of Adjourned Meetings.** Any meeting of stockholders, whether annual or special, may be adjourned from time to time either by the chairman of the meeting or by the vote of a majority of the shares present in person, by remote communication, if applicable, or represented by proxy. When a meeting is adjourned to another time or place, if any, notice need not be given of the adjourned meeting if the time and place, if any, thereof are announced at the meeting at which the adjournment is taken. At the adjourned meeting, the corporation may transact any business which might have been transacted at the original meeting. If the adjournment is for more than thirty (30) days or if after the adjournment a new record date is fixed for the adjourned meeting, a notice of the adjourned meeting shall be given to each stockholder of record entitled to vote at the meeting.

**Section 10. Voting Rights.** For the purpose of determining those stockholders entitled to vote at any meeting of the stockholders, except as otherwise provided by law, only persons in whose names shares stand on the stock records of the corporation on the record date,

as provided in Section 12 of these Bylaws, shall be entitled to vote at any meeting of stockholders. Every person entitled to vote or execute consents shall have the right to do so either in person, by remote communication, if applicable, or by an agent or agents authorized by a proxy granted in accordance with Delaware law. An agent so appointed need not be a stockholder. No proxy shall be voted after three (3) years from its date of creation unless the proxy provides for a longer period.

**Section 11. Joint Owners of Stock.** If shares or other securities having voting power stand of record in the names of two (2) or more persons, whether fiduciaries, members of a partnership, joint tenants, tenants in common, tenants by the entirety, or otherwise, or if two (2) or more persons have the same fiduciary relationship respecting the same shares, unless the Secretary is given written notice to the contrary and is furnished with a copy of the instrument or order appointing them or creating the relationship wherein it is so provided, their acts with respect to voting shall have the following effect: (a) if only one (1) votes, his act binds all; (b) if more than one (1) votes, the act of the majority so voting binds all; (c) if more than one (1) votes, but the vote is evenly split on any particular matter, each faction may vote the securities in question proportionally, or may apply to the Delaware Court of Chancery for relief as provided in the DGCL, Section 217(b). If the instrument filed with the Secretary shows that any such tenancy is held in unequal interests, a majority or even-split for the purpose of subsection (c) shall be a majority or even-split in interest

**Section 12. List of Stockholders.** The Secretary shall prepare and make, at least ten (10) days before every meeting of stockholders, a complete list of the stockholders entitled to vote at said meeting, arranged in alphabetical order, showing the address of each stockholder and the number of shares registered in the name of each stockholder. Such list shall be open to the examination of any stockholder, for any purpose germane to the meeting, on a reasonably accessible electronic network, provided that the information required to gain access to such list is provided with the notice of the meeting, or during ordinary business hours, at the principal place of business of the corporation. In the event that the corporation determines to make the list available on an electronic network, the corporation may take reasonable steps to ensure that such information is available only to stockholders of the corporation. The list shall be open to examination of any stockholder during the time of the meeting as provided by law.

**Section 13. Action Without Meeting.**

(a) Unless otherwise provided in the Certificate of Incorporation, any action required by statute to be taken at any annual or special meeting of the stockholders, or any action which may be taken at any annual or special meeting of the stockholders, may be taken without a meeting, without prior notice and without a vote, if a consent in writing, or by electronic transmission setting forth the action so taken, shall be signed by the holders of outstanding stock having not less than the minimum number of votes that would be necessary to authorize or take such action at a meeting at which all shares entitled to vote thereon were present and voted.

(b) Every written consent or electronic transmission shall bear the date of signature of each stockholder who signs the consent, and no written consent or electronic transmission shall be effective to take the corporate action referred to therein unless, within sixty (60) days of the earliest dated consent delivered to the corporation in the manner herein required,

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written consents or electronic transmissions signed by a sufficient number of stockholders to take action are delivered to the corporation by delivery to its registered office in the State of Delaware, its principal place of business or an officer or agent of the corporation having custody of the book in which proceedings of meetings of stockholders are recorded. Delivery made to a corporation's registered office shall be by hand or by certified or registered mail, return receipt requested.

(c) Prompt notice of the taking of the corporate action without a meeting by less than unanimous written consent shall be given to those stockholders who have not consented in writing or by electronic transmission and who, if the action had been taken at a meeting, would have been entitled to notice of the meeting if the record date for such meeting had been the date that written consents signed by a sufficient number of stockholders to take action were delivered to the corporation as provided in Section 228(c) of the DGCL. If the action which is consented to is such as would have required the filing of a certificate under any section of the DGCL if such action had been voted on by stockholders at a meeting thereof, then the certificate filed under such section shall state, in lieu of any statement required by such section concerning any vote of stockholders, that written consent has been given in accordance with Section 228 of the DGCL.

(d) A telegram, cablegram or other electronic transmission consenting to an action to be taken and transmitted by a stockholder or proxyholder, shall be deemed to be written, signed and dated for the purposes of this section, provided that any such telegram, cablegram or other electronic transmission sets forth or is delivered with information from which the corporation can determine (i) that the telegram, cablegram or other electronic transmission was transmitted by the stockholder or proxyholder or by a person or persons authorized to act for the stockholder and (ii) the date on which such stockholder or proxyholder or authorized person or persons transmitted such telegram, cablegram or electronic transmission. The date on which such telegram, cablegram or electronic transmission is transmitted shall be deemed to be the date on which such consent was signed. No consent given by telegram, cablegram or other electronic transmission shall be deemed to have been delivered until such consent is reproduced in paper form and until such paper form shall be delivered to the corporation by delivery to its registered office in the state of Delaware, its principal place of business or an officer or agent of the corporation having custody of the book in which proceedings of meetings of stockholders are recorded. Delivery made to a corporation's registered office shall be made by hand or by certified or registered mail, return receipt requested. Notwithstanding the foregoing limitations on delivery, consents given by telegram, cablegram or other electronic transmission may be otherwise delivered to the principal place of business of the corporation or to an officer or agent of the corporation having custody of the book in which proceedings of meetings of stockholders are recorded if, to the extent and in the manner provided by resolution of the board of directors of the corporation. Any copy, facsimile or other reliable reproduction of a consent in writing may be substituted or used in lieu of the original writing for any and all purposes for which the original writing could be used, provided that such copy, facsimile or other reproduction shall be a complete reproduction of the entire original writing.

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**Section 14. Organization.**

(a) At every meeting of stockholders, the Chairman of the Board of Directors, or, if a Chairman has not been appointed or is absent, the President, or, if the President is absent, chairman of the meeting chosen by a majority in interest of the stockholders entitled to vote, present in person or by proxy, shall act as chairman. The Secretary, or, in his absence, an Assistant Secretary directed to do so by the President, shall act as secretary of the meeting.

(b) The Board of Directors of the corporation shall be entitled to make such rules or regulations for the conduct of meetings of stockholders as it shall deem necessary, appropriate or convenient. Subject to such rules and regulations of the Board of Directors, if any, the chairman of the meeting shall have the right and authority to prescribe such rules, regulations and procedures and to do all such acts as, in the judgment of such chairman, are necessary, appropriate or convenient for the proper conduct of the meeting, including, without limitation, establishing an agenda or order of business for the meeting, rules and procedures for maintaining order at the meeting and the safety of those present, limitations on participation in such meeting to stockholders of record of the corporation and their duly authorized and constituted proxies and such other persons as the chairman shall permit, restrictions on entry to the meeting after the time fixed for the commencement thereof, limitations on the time allotted to questions or comments by participants and regulation of the opening and closing of the polls for balloting on matters which are to be voted on by ballot. The date and time of the opening and closing of the polls for each matter upon which the stockholders will vote at the meeting shall be announced at the meeting. Unless and to the extent determined by the Board of Directors or the chairman of the meeting, meetings of stockholders shall not be required to be held in accordance with rules of parliamentary procedure.

## ARTICLE IV

### DIRECTORS

#### Section 15. Number and Term of Office.

The authorized number of directors of the corporation shall be fixed by the Board of Directors from time to time. Directors need not be stockholders unless so required by the Certificate of Incorporation. If for any cause, the directors shall not have been elected at an annual meeting, they may be elected as soon thereafter as convenient.

**Section 16. Powers.** The powers of the corporation shall be exercised, its business conducted and its property controlled by the Board of Directors, except as may be otherwise provided by statute or by the Certificate of Incorporation.

#### Section 17. Term of Directors.

(a) Subject to the rights of the holders of any series of Preferred Stock to elect additional directors under specified circumstances, directors shall be elected at each annual meeting of stockholders for a term of one year. Each director shall serve until his successor is duly elected and qualified or until his death, resignation or removal. No decrease in the number of directors constituting the Board of Directors shall shorten the term of any incumbent director.

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(b) No person entitled to vote at an election for directors may cumulate votes to which such person is entitled, unless, at the time of such election, the corporation is subject to Section 2115(b) of the CGCL. During such time or times that the corporation is subject to Section 2115(b) of the CGCL, every stockholder entitled to vote at an election for directors may cumulate such stockholder's votes and give one candidate a number of votes equal to the number of directors to be elected multiplied by the number of votes to which such stockholder's shares are otherwise entitled, or distribute the stockholder's votes on the same principle among as many candidates as such stockholder thinks fit. No stockholder, however, shall be entitled to so cumulate such stockholder's votes unless (i) the names of such candidate or candidates have been placed in nomination prior to the voting and (ii) the stockholder has given notice at least ten (10) days prior to the meeting, of such stockholder's intention to cumulate such stockholder's votes. If any stockholder has given proper notice to cumulate votes, all stockholders may cumulate their votes for any candidates who have been properly placed in nomination. Under cumulative voting, the candidates receiving the highest number of votes, up to the number of directors to be elected, are elected.

#### Section 18. Vacancies.

(a) Unless otherwise provided in the Certificate of Incorporation, and subject to the rights of the holders of any series of Preferred Stock, any vacancies on the Board of Directors resulting from death, resignation, disqualification, removal or other causes and any newly created directorships resulting from any increase in the number of directors shall, unless the Board of Directors determines by resolution that any such vacancies or newly created directorships shall be filled by stockholders, be filled only by the affirmative vote of a majority of the directors then in office, even though less than a quorum of the Board of Directors, or by a sole remaining director, *provided, however*, that whenever the holders of any class or classes of stock or series thereof are entitled to elect one or more directors by the provisions of the Certificate of Incorporation, vacancies and newly created directorships of such class or classes or series shall, unless the Board of Directors determines by resolution that any such vacancies or newly created directorships shall be filled by stockholders, be filled by a majority of the directors elected by such class or classes or series thereof then in office, or by a sole remaining director so elected. Any director elected in accordance with the preceding sentence shall hold office for the remainder of the full term of the director for which the vacancy was created or occurred and until such director's successor shall have been elected and qualified. A vacancy in the Board of Directors shall be deemed to exist under this Bylaw in the case of the death, removal or resignation of any director.

(b) At any time or times that the corporation is subject to §2115(b) of the CGCL, if, after the filling of any vacancy, the directors then in office who have been elected by stockholders shall constitute less than a majority of the directors then in office, then

(i) any holder or holders of an aggregate of five percent (5%) or more of the total number of shares at the time outstanding having the right to vote for those directors may call a special meeting of stockholders; or

(ii) the Superior Court of the proper county shall, upon application of such stockholder or stockholders, summarily order a special meeting of the stockholders, to be held to

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elect the entire board, all in accordance with Section 305(c) of the CGCL, the term of office of any director shall terminate upon that election of a successor.

**Section 19. Resignation.** Any director may resign at any time by delivering his or her notice in writing or by electronic transmission to the Secretary, such resignation to specify whether it will be effective at a particular time, upon receipt by the Secretary or at the pleasure of the Board of Directors. If no such specification is made, it shall be deemed effective at the pleasure of the Board of Directors. When one or more directors shall resign from the Board of Directors, effective at a future date, a majority of the directors then in office, including those who have so resigned, shall have power to fill such vacancy or vacancies, the vote thereon to take effect when such resignation or resignations shall become effective, and each Director so chosen shall hold office for the unexpired portion of the term of the Director whose place shall be vacated and until his successor shall have been duly elected and qualified.

#### Section 20. Removal.

(a) Subject to any limitations imposed by applicable law and unless otherwise provided in the Certificate of Incorporation, (and assuming the corporation is not subject to Section 2115 of the CGCL), the Board of Directors or any director may be removed from office at any time (i) with cause by the affirmative vote of the holders of a majority of the voting power of all then-outstanding shares of capital stock of the corporation entitled to vote generally at an election of directors or (ii) without cause by the affirmative vote of the holders of a majority of the voting power of all then-outstanding shares of capital stock of the corporation, entitled to vote generally at an election of directors,

(b) During such time or times that the corporation is subject to Section 2115(b) of the CGCL, the Board of Directors or any individual director may be removed from office at any time without cause by the affirmative vote of the holders of at least a majority of the outstanding shares entitled to vote

on such removal; provided, however, that unless the entire Board is removed, no individual director may be removed when the votes cast against such director's removal, or not consenting in writing to such removal, would be sufficient to elect that director if voted cumulatively at an election which the same total number of votes were cast (or, if such action is taken by written consent, all shares entitled to vote were voted) and the entire number of directors authorized at the time of such director's most recent election were then being elected.

## **Section 21. Meetings**

(a) **Regular Meetings.** Unless otherwise restricted by the Certificate of Incorporation, regular meetings of the Board of Directors may be held at any time or date and at any place within or without the State of Delaware which has been designated by the Board of Directors and publicized among all directors, either orally or in writing, including a voice-messaging system or other system designated to record and communicate messages, facsimile, telegraph or telex, or by electronic mail or other electronic means. No further notice shall be required for a regular meeting of the Board of Directors.

(b) **Special Meetings.** Unless otherwise restricted by the Certificate of Incorporation, special meetings of the Board of Directors may be held at any time and place

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within or without the State of Delaware whenever called by the Chairman of the Board, the President or any two of the directors.

(c) **Meetings by Electronic Communications Equipment.** Any member of the Board of Directors, or of any committee thereof, may participate in a meeting by means of conference telephone or other communications equipment by means of which all persons participating in the meeting can hear each other, and participation in a meeting by such means shall constitute presence in person at such meeting.

(d) **Notice of Special Meetings.** Notice of the time and place of all special meetings of the Board of Directors shall be orally or in writing, by telephone, including a voice messaging system or other system or technology designed to record and communicate messages, facsimile, telegraph or telex, by nationally recognized overnight courier, or by electronic mail or other electronic means, during normal business hours, at least twenty-four (24) hours before the date and time of the meeting. If notice is sent by US mail, it shall be sent by first class mail, postage prepaid at least three (3) days before the date of the meeting. If notice is sent by a nationally recognized overnight courier, it shall be sent, prepaid, at least two (2) days before the date of the meeting. Notice of any meeting may be waived in writing or by electronic transmission at any time before or after the meeting and will be waived by any director by attendance thereat, except when the director attends the meeting for the express purpose of objecting, at the beginning of the meeting, to the transaction of any business because the meeting is not lawfully called or convened.

(e) **Waiver of Notice.** The transaction of all business at any meeting of the Board of Directors, or any committee thereof, however called or noticed, or wherever held, shall be as valid as though had at a meeting duly held after regular call and notice, if a quorum be present and if, either before or after the meeting, each of the directors not present who did not receive notice shall sign a written waiver of notice or shall waive notice by electronic transmission. All such waivers shall be filed with the corporate records or made a part of the minutes of the meeting.

## **Section 22. Quorum and Voting.**

(a) Unless the Certificate of Incorporation requires a greater number, a quorum of the Board of Directors shall consist of a majority of the exact number of directors fixed from time to time by the Board of Directors in accordance with the Certificate of Incorporation; *provided, however*, at any meeting, whether a quorum be present or otherwise, a majority of the directors present may adjourn from time to time until the time fixed for the next regular meeting of the Board of Directors, without notice other than by announcement at the meeting.

(b) At each meeting of the Board of Directors at which a quorum is present, all questions and business shall be determined by the affirmative vote of a majority of the directors present, unless a different vote be required by law, the Certificate of Incorporation or these Bylaws.

**Section 23. Action Without Meeting.** Unless otherwise restricted by the Certificate of Incorporation or these Bylaws, any action required or permitted to be taken at any meeting of

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the Board of Directors or of any committee thereof may be taken without a meeting, if all members of the Board of Directors or committee, as the case may be, consent thereto in writing or by electronic transmission, and such writing or writings or transmission or transmissions are filed with the minutes of proceedings of the Board of Directors or committee. Such filing shall be in paper form if the minutes are maintained in paper form and shall be in electronic form if the minutes are maintained in electronic form.

**Section 24. Fees and Compensation.** Directors shall be entitled to such compensation for their services as may be approved by the Board of Directors, including, if so approved, by resolution of the Board of Directors, a fixed sum and expenses of attendance, if any, for attendance at each regular or special meeting of the Board of Directors and at any meeting of a committee of the Board of Directors. Nothing herein contained shall be construed to preclude any director from serving the corporation in any other capacity as an officer, agent, employee, or otherwise and receiving compensation therefor.

## **Section 25. Committees.**

(a) **Executive Committee.** The Board of Directors may appoint an Executive Committee to consist of three (3) or more members of the Board of Directors. The Executive Committee, to the extent permitted by law and provided in the resolution of the Board of Directors shall have and may exercise all the powers and authority of the Board of Directors in the management of the business and affairs of the corporation, and may authorize the seal of the corporation to be affixed to all papers which may require it; but no such committee shall have the power or authority in reference to (i) approving or adopting, or recommending to the stockholders, any action or matter expressly required by the DGCL to be submitted to stockholders for approval, or (ii) adopting, amending or repealing any bylaw of the corporation.

(b) **Other Committees.** The Board of Directors may, from time to time, appoint such other committees as may be permitted by law. Such other committees appointed by the Board of Directors shall consist of three (3) or more members of the Board of Directors and shall have such powers and perform such duties as may be prescribed by the resolution or resolutions creating such committees, but in no event shall any such committee have the powers denied to the Executive Committee in these Bylaws.

(c) **Term.** The Board of Directors, subject to any requirements of any outstanding series of Preferred Stock and the provisions of subsections (a) or (b) of this Bylaw may at any time increase or decrease the number of members of a committee or terminate the existence of a committee. The membership of a committee member shall terminate on the date of his death or voluntary resignation from the committee or from the Board of Directors. The Board of Directors may at any time for any reason remove any individual committee member and the Board of Directors may fill any committee vacancy created by death, resignation, removal or increase in the number of members of the committee. The Board of Directors may designate one or more directors as alternate members of any committee, who may replace any absent or disqualified member at any meeting of the committee, and, in addition, in the absence or disqualification of any member of a committee, the member or members thereof present at any meeting and not disqualified from voting, whether or not he or they constitute a quorum, may

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unanimously appoint another member of the Board of Directors to act at the meeting in the place of any such absent or disqualified member.

(d) **Meetings.** Unless the Board of Directors shall otherwise provide, regular meetings of the Executive Committee or any other committee appointed pursuant to this Section 25 shall be held at such times and places as are determined by the Board of Directors, or by any such committee, and when notice thereof has been given to each member of such committee, no further notice of such regular meetings need be given thereafter. Special meetings of any such committee may be held at any place which has been determined from time to time by such committee, and may be called by any director who is a member of such committee, upon notice to the members of such committee of the time and place of such special meeting given in the manner provided for the giving of notice to members of the Board of Directors of the time and place of special meetings of the Board of Directors. Notice of any special meeting of any committee may be waived in writing at any time before or after the meeting and will be waived by any director by attendance thereat, except when the director attends such special meeting for the express purpose of objecting, at the beginning of the meeting, to the transaction of any business because the meeting is not lawfully called or convened. Unless otherwise provided by the Board of Directors in the resolutions authorizing the creation of the committee, a majority of the authorized number of members of any such committee shall constitute a quorum for the transaction of business, and the act of a majority of those present at any meeting at which a quorum is present shall be the act of such committee.

**Section 26. Organization.** At every meeting of the directors, the Chairman of the Board of Directors, or, if a Chairman has not been appointed or is absent, the President, or if the President is absent, the most senior Vice President, (if a director) or, in the absence of any such person, a chairman of the meeting chosen by a majority of the directors present, shall preside over the meeting. The Secretary, or in his absence, any Assistant Secretary directed to do so by the President, shall act as secretary of the meeting.

## ARTICLE V

### OFFICERS

**Section 27. Officers Designated.** The officers of the corporation shall include, if and when designated by the Board of Directors, the Chairman of the Board of Directors, the Chief Executive Officer, the President, one or more Vice Presidents, the Secretary, the Chief Financial Officer, the Treasurer and the Controller, all of whom shall be elected at the annual organizational meeting of the Board of Directors. The Board of Directors may also appoint one or more Assistant Secretaries, Assistant Treasurers, Assistant Controllers and such other officers and agents with such powers and duties as it shall deem necessary. The Board of Directors may assign such additional titles to one or more of the officers as it shall deem appropriate. Any one person may hold any number of offices of the corporation at any one time unless specifically prohibited therefrom by law. The salaries and other compensation of the officers of the corporation shall be fixed by or in the manner designated by the Board of Directors.

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### **Section 28. Tenure and Duties of Officers.**

(a) **General.** All officers shall hold office at the pleasure of the Board of Directors and until their successors shall have been duly elected and qualified, unless sooner removed. Any officer elected or appointed by the Board of Directors may be removed at any time by the Board of Directors. If the office of any officer becomes vacant for any reason, the vacancy may be filled by the Board of Directors.

(b) **Duties of Chairman of the Board of Directors.** The Chairman of the Board of Directors, when present, shall preside at all meetings of the stockholders and the Board of Directors. The Chairman of the Board of Directors shall perform other duties commonly incident to the office and shall also perform such other duties and have such other powers as the Board of Directors shall designate from time to time. If there is no President, then the Chairman of the Board of Directors shall also serve as the Chief Executive Officer of the corporation and shall have the powers and duties prescribed in paragraph (c) of this Section 28.

(c) **Duties of President.** The President shall preside at all meetings of the stockholders and at all meetings of the Board of Directors, unless the Chairman of the Board of Directors has been appointed and is present. Unless some other officer has been elected Chief Executive Officer of the corporation, the President shall be the chief executive officer of the corporation and shall, subject to the control of the Board of Directors, have general supervision, direction and control of the business and officers of the corporation. The President shall perform other duties commonly incident to the office and shall also perform such other duties and have such other powers as the Board of Directors shall designate from time to time.

(d) **Duties of Vice Presidents.** The Vice Presidents may assume and perform the duties of the President in the absence or disability of the President or whenever the office of President is vacant. The Vice Presidents shall perform other duties commonly incident to their office and shall also perform such other duties and have such other powers as the Board of Directors or the President shall designate from time to time.

(e) **Duties of Secretary.** The Secretary shall attend all meetings of the stockholders and of the Board of Directors and shall record all acts and proceedings thereof in the minute book of the corporation. The Secretary shall give notice in conformity with these Bylaws of all meetings of the stockholders and of all meetings of the Board of Directors and any committee thereof requiring notice. The Secretary shall perform all other duties provided for in these Bylaws and other duties commonly incident to the office and shall also perform such other duties and have such other powers as the Board of Directors shall designate from time to time. The President may direct any Assistant Secretary to assume and perform the duties of the Secretary in the absence or disability of the Secretary, and each Assistant Secretary shall perform other duties commonly incident to the office and shall also perform such other duties and have such other powers as the Board of Directors or the President shall designate from time to time.

(f) **Duties of Chief Financial Officer.** The Chief Financial Officer shall keep or cause to be kept the books of account of the corporation in a thorough and proper manner and shall render statements of the financial affairs of the corporation in such form and as often as required by the Board of Directors or

order of the Board of Directors, shall have the custody of all funds and securities of the corporation. The Chief Financial Officer shall perform other duties commonly incident to his office and shall also perform such other duties and have such other powers as the Board of Directors or the President shall designate from time to time. The President may direct the Treasurer or any Assistant Treasurer, or the Controller or any Assistant Controller to assume and perform the duties of the Chief Financial Officer in the absence or disability of the Chief Financial Officer, and each Treasurer and Assistant Treasurer and each Controller and Assistant Controller shall perform other duties commonly incident to the office and shall also perform such other duties and have such other powers as the Board of Directors or the President shall designate from time to time.

**Section 29. Delegation of Authority.** The Board of Directors may from time to time delegate the powers or duties of any officer to any other officer or agent, notwithstanding any provision hereof.

**Section 30. Resignations.** Any officer may resign at any time by giving notice in writing or by electronic transmission notice to the Board of Directors or to the President or to the Secretary. Any such resignation shall be effective when received by the person or persons to whom such notice is given, unless a later time is specified therein, in which event the resignation shall become effective at such later time. Unless otherwise specified in such notice, the acceptance of any such resignation shall not be necessary to make it effective. Any resignation shall be without prejudice to the rights, if any, of the corporation under any contract with the resigning officer.

**Section 31. Removal.** Any officer may be removed from office at any time, either with or without cause, by the affirmative vote of a majority of the directors in office at the time, or by the unanimous written consent of the directors in office at the time, or by any committee or superior officers upon whom such power of removal may have been conferred by the Board of Directors.

## ARTICLE VI

### EXECUTION OF CORPORATE INSTRUMENTS AND VOTING OF SECURITIES OWNED BY THE CORPORATION

**Section 32. Execution of Corporate Instruments.** The Board of Directors may, in its discretion, determine the method and designate the signatory officer or officers, or other person or persons, to execute on behalf of the corporation any corporate instrument or document, or to sign on behalf of the corporation the corporate name without limitation, or to enter into contracts on behalf of the corporation, except where otherwise provided by law or these Bylaws, and such execution or signature shall be binding upon the corporation.

All checks and drafts drawn on banks or other depositories on funds to the credit of the corporation or in special accounts of the corporation shall be signed by such person or persons as the Board of Directors shall authorize so to do.

Unless authorized or ratified by the Board of Directors or within the agency power of an officer, no officer, agent or employee shall have any power or authority to bind the corporation

by any contract or engagement or to pledge its credit or to render it liable for any purpose or for any amount.

**Section 33. Voting of Securities Owned by the Corporation.** All stock and other securities of other corporations owned or held by the corporation for itself, or for other parties in any capacity, shall be voted, and all proxies with respect thereto shall be executed, by the person authorized so to do by resolution of the Board of Directors, or, in the absence of such authorization, by the Chairman of the Board of Directors, the Chief Executive Officer, the President, or any Vice President.

## ARTICLE VII

### SHARES OF STOCK

**Section 34. Form and Execution of Certificates.** Certificates for the shares of stock of the corporation shall be in such form as is consistent with the Certificate of Incorporation and applicable law. Every holder of stock in the corporation shall be entitled to have a certificate signed by or in the name of the corporation by the Chairman of the Board of Directors, or the President or any Vice President and by the Treasurer or Assistant Treasurer or the Secretary or Assistant Secretary, certifying the number of shares owned by him in the corporation. Any or all of the signatures on the certificate may be facsimiles. In case any officer, transfer agent, or registrar who has signed or whose facsimile signature has been placed upon a certificate shall have ceased to be such officer, transfer agent, or registrar before such certificate is issued, it may be issued with the same effect as if he were such officer, transfer agent, or registrar at the date of issue. Each certificate shall state upon the face or back thereof, in full or in summary, all of the powers, designations, preferences, and rights, and the limitations or restrictions of the shares authorized to be issued or shall, except as otherwise required by law, set forth on the face or back a statement that the corporation will furnish without charge to each stockholder who so requests the powers, designations, preferences and relative, participating, optional, or other special rights of each class of stock or series thereof and the qualifications, limitations or restrictions of such preferences and/or rights. Within a reasonable time after the issuance or transfer of uncertificated stock, the corporation shall send to the registered owner thereof a written notice containing the information required to be set forth or stated on certificates pursuant to this section or otherwise required by law or with respect to this section a statement that the corporation will furnish without charge to each stockholder who so requests the powers, designations, preferences and relative participating, optional or other special rights of each class of stock or series thereof and the qualifications, limitations or restrictions of such preferences and/or rights.

**Section 35. Lost Certificates.** A new certificate or certificates shall be issued in place of any certificate or certificates theretofore issued by the corporation alleged to have been lost, stolen, or destroyed, upon the making of an affidavit of that fact by the person claiming the certificate of stock to be lost, stolen, or destroyed. The corporation may require, as a condition precedent to the issuance of a new certificate or certificates, the owner of such lost, stolen, or destroyed certificate or certificates, or the owner's legal representative, to agree to indemnify the corporation in such manner as it shall require or to give the corporation a surety bond in such



form and amount as it may direct as indemnity against any claim that may be made against the corporation with respect to the certificate alleged to have been lost, stolen, or destroyed.

**Section 36. Transfers.**

(a) Transfers of record of shares of stock of the corporation shall be made only upon its books by the holders thereof, in person or by attorney duly authorized, and upon the surrender of a properly endorsed certificate or certificates for a like number of shares.

(b) The corporation shall have power to enter into and perform any agreement with any number of stockholders of any one or more classes of stock of the corporation to restrict the transfer of shares of stock of the corporation of any one or more classes owned by such stockholders in any manner not prohibited by the DGCL.

**Section 37. Fixing Record Dates.**

(a) In order that the corporation may determine the stockholders entitled to notice of or to vote at any meeting of stockholders or any adjournment thereof, the Board of Directors may fix, in advance, a record date, which record date shall not precede the date upon which the resolution fixing the record date is adopted by the Board of Directors, and which record date shall, subject to applicable law, not be more than sixty (60) nor less than ten (10) days before the date of such meeting. If no record date is fixed by the Board of Directors, the record date for determining stockholders entitled to notice of or to vote at a meeting of stockholders shall be at the close of business on the day next preceding the day on which notice is given, or if notice is waived, at the close of business on the day next preceding the day on which the meeting is held. A determination of stockholders of record entitled to notice of or to vote at a meeting of stockholders shall apply to any adjournment of the meeting; *provided, however*, that the Board of Directors may fix a new record date for the adjourned meeting.

(b) In order that the corporation may determine the stockholders entitled to consent to corporate action in writing without a meeting, the Board of Directors may fix a record date, which record date shall not precede the date upon which the resolution fixing the record date is adopted by the Board of Directors, and which date shall not be more than ten (10) days after the date upon which the resolution fixing the record date is adopted by the Board of Directors. Any stockholder of record seeking to have the stockholders authorize or take corporate action by written consent shall, by written notice to the Secretary, request the Board of Directors to fix a record date. The Board of Directors shall promptly, but in all events within ten (10) days after the date on which such a request is received, adopt a resolution fixing the record date. If no record date has been fixed by the Board of Directors within ten (10) days of the date on which such a request is received, the record date for determining stockholders entitled to consent to corporate action in writing without a meeting, when no prior action by the Board of Directors is required by applicable law, shall be the first date on which a signed written consent setting forth the action taken or proposed to be taken is delivered to the corporation by delivery to its registered office in the State of Delaware, its principal place of business or an officer or agent of the corporation having custody of the book in which proceedings of meetings of stockholders are recorded. Delivery made to the corporation's registered office shall be by hand, by certified or registered mail, return receipt requested, or by a nationally recognized overnight

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courier. If no record date has been fixed by the Board of Directors and prior action by the Board of Directors is required by law, the record date for determining stockholders entitled to consent to corporate action in writing without a meeting shall be at the close of business on the day on which the Board of Directors adopts the resolution taking such prior action.

(c) In order that the corporation may determine the stockholders entitled to receive payment of any dividend or other distribution or allotment of any rights or the stockholders entitled to exercise any rights in respect of any change, conversion or exchange of stock, or for the purpose of any other lawful action, the Board of Directors may fix, in advance, a record date, which record date shall not precede the date upon which the resolution fixing the record date is adopted, and which record date shall be not more than sixty (60) days prior to such action. If no record date is fixed, the record date for determining stockholders for any such purpose shall be at the close of business on the day on which the Board of Directors adopts the resolution relating thereto.

**Section 38. Registered Stockholders.** The corporation shall be entitled to recognize the exclusive right of a person registered on its books as the owner of shares to receive dividends, and to vote as such owner, and shall not be bound to recognize any equitable or other claim to or interest in such share or shares on the part of any other person whether or not it shall have express or other notice thereof, except as otherwise provided by the laws of Delaware.

**ARTICLE VIII**

**OTHER SECURITIES OF THE CORPORATION**

**Section 39. Execution of Other Securities.** All bonds, debentures and other corporate securities of the corporation, other than stock certificates (covered in Section 34), may be signed by the Chairman of the Board of Directors, the President or any Vice President, or such other person as may be authorized by the Board of Directors, and the corporate seal unpressed thereon or a facsimile of such seal imprinted thereon and attested by the signature of the Secretary or an Assistant Secretary, or the Chief Financial Officer or Treasurer or an Assistant Treasurer; *provided, however*, that where any such bond, debenture or other corporate security shall be authenticated by the manual signature, or where permissible facsimile signature, of a trustee under an indenture pursuant to which such bond, debenture or other corporate security shall be issued, the signatures of the persons signing and attesting the corporate seal on such bond, debenture or other corporate security may be the imprinted facsimile of the signatures of such persons. Interest coupons appertaining to any such bond, debenture or other corporate security, authenticated by a trustee as aforesaid, shall be signed by the Treasurer or an Assistant Treasurer of the corporation or such other person as may be authorized by the Board of Directors, or bear imprinted thereon the facsimile signature of such person. In case any officer who shall have signed or attested any bond, debenture or other corporate security, or whose facsimile signature shall appear thereon or on any such interest coupon, shall have ceased to be such officer before the bond, debenture or other corporate security so signed or attested shall have been delivered, such bond, debenture or other corporate security nevertheless may be adopted by the corporation and issued and delivered as though the person who signed the same or whose facsimile signature shall have been used thereon had not ceased to be such officer of the corporation.

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**ARTICLE IX**

## DIVIDENDS

**Section 40. Declaration of Dividends.** Dividends upon the capital stock of the corporation, subject to the provisions of the Certificate of Incorporation and applicable law, if any, may be declared by the Board of Directors pursuant to law at any regular or special meeting. Dividends may be paid in cash, in property, or in shares of the capital stock, subject to the provisions of the Certificate of Incorporation and applicable law.

**Section 41. Dividend Reserve.** Before payment of any dividend, there may be set aside out of any funds of the corporation available for dividends such sum or sums as the Board of Directors from time to time, in their absolute discretion, think proper as a reserve or reserves to meet contingencies, or for equalizing dividends, or for repairing or maintaining any property of the corporation, or for such other purpose as the Board of Directors shall think conducive to the interests of the corporation, and the Board of Directors may modify or abolish any such reserve in the manner in which it was created.

## ARTICLE X

### FISCAL YEAR

**Section 42. Fiscal Year.** The fiscal year of the corporation shall be fixed by resolution of the Board of Directors.

## ARTICLE XI

### INDEMNIFICATION

**Section 43. Indemnification of Directors, Other Officers, Employees and Other Agents.**

(a) **Directors and Officers.** The corporation shall indemnify its directors and officers to the fullest extent not prohibited by the DGCL or any other applicable law; *provided, however*, that the corporation may modify the extent of such indemnification by individual contracts with its directors and officers; and, *provided, further*, that the corporation shall not be required to indemnify any director or officer in connection with any proceeding (or part thereof) initiated by such person unless (i) such indemnification is expressly required to be made by law, (ii) the proceeding was authorized by the Board of Directors of the corporation, (iii) such indemnification is provided by the corporation, in its sole discretion, pursuant to the powers vested in the corporation under the Delaware General Corporation Law or any other applicable law or (iv) such indemnification is required to be made under subsection (d).

(b) **Employees and Other Agents.** The corporation shall have power to indemnify its employees and other agents as set forth in the DGCL or any other applicable law. The Board of Directors shall have the power to delegate the determination of whether indemnification shall be given to any such person to such officers or other persons as the Board of Directors shall determine.

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(c) **Expenses.** The corporation shall advance to any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative, by reason of the fact that he is or was a director or officer, of the corporation, or is or was serving at the request of the corporation as a director or officer of another corporation, partnership, joint venture, trust or other enterprise, prior to the final disposition of the proceeding, promptly following request therefor, all expenses incurred by any director or officer in connection with such proceeding, *provided, however*, that, if the DGCL requires, an advancement of expenses incurred by a director or officer in his or her capacity as a director or officer (and not in any other capacity in which service was or is rendered by such indemnitee, including, without limitation, service to an employee benefit plan) shall be made only upon delivery to the corporation of an undertaking, by or on behalf of such indemnitee, to repay all amounts so advanced if it shall ultimately be determined by final judicial decision from which there is no further right to appeal that such indemnitee is not entitled to be indemnified for such expenses under this Section 43 or otherwise.

Notwithstanding the foregoing, unless otherwise determined pursuant to paragraph (e) of this Bylaw, no advance shall be made by the corporation to an officer of the corporation (except by reason of the fact that such officer is or was a director of the corporation, in which event this paragraph shall not apply) in any action, suit or proceeding, whether civil, criminal, administrative or investigative, if a determination is reasonably and promptly made (i) by a majority vote of a quorum consisting of directors who were not parties to the proceeding, even if not a quorum, or (ii) by a committee of such directors designated by a majority of such directors, even though less than a quorum, or (iii) if there are no such directors, or such directors so direct, by independent legal counsel in a written opinion, that the facts known to the decision-making party at the time such determination is made demonstrate clearly and convincingly that such person acted in bad faith or in a manner that such person did not believe to be in or not opposed to the best interests of the corporation.

(d) **Enforcement.** Without the necessity of entering into an express contract, all rights to indemnification and advances to directors and officers under this Bylaw shall be deemed to be contractual rights and be effective to the same extent and as if provided for in a contract between the corporation and the director or officer. Any right to indemnification or advances granted by this Bylaw to a director or officer shall be enforceable by or on behalf of the person holding such right in any court of competent jurisdiction if (i) the claim for indemnification or advances is denied, in whole or in part, or (ii) no disposition of such claim is made within ninety (90) days of request therefor. The claimant in such enforcement action, if successful in whole or in part, shall be entitled to be paid also the expense of prosecuting the claim. In connection with any claim for indemnification, the corporation shall be entitled to raise as a defense to any such action that the claimant has not met the standards of conduct that make it permissible under the DGCL or any other applicable law for the corporation to indemnify the claimant for the amount claimed. In connection with any claim by an officer of the corporation (except in any action, suit or proceeding, whether civil, criminal, administrative or investigative, by reason of the fact that such officer is or was a director of the corporation) for advances, the corporation shall be entitled to raise a defense as to any such action clear and convincing evidence that such person acted in bad faith or in a manner that such person did not believe to be in or not opposed to the best interests of the corporation, or with respect to any criminal action or proceeding that such person acted without reasonable cause to believe that his conduct was

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lawful. Neither the failure of the corporation (including its Board of Directors, independent legal counsel or its stockholders) to have made a determination prior to the commencement of such action that indemnification of the claimant is proper in the circumstances because he has met the applicable standard of conduct set forth in the DGCL or any other applicable law, nor an actual determination by the corporation (including its Board of Directors, independent legal counsel or its stockholders) that the claimant has not met such applicable standard of conduct, shall be a defense to the action or create a presumption that claimant has not met the applicable standard of conduct. In any suit brought by a director or officer to enforce a right to indemnification or to an advancement of expenses hereunder, the burden of proving that the director or officer is not entitled to be indemnified, or to such advancement of expenses, under this Article XI or otherwise shall be on the corporation.

(e) **Non-Exclusivity of Rights.** The rights conferred on any person by this Bylaw shall not be exclusive of any other right which such person may have or hereafter acquire under any applicable statute, provision of the Certificate of Incorporation, Bylaws, agreement, vote of stockholders or disinterested directors or otherwise, both as to action in his official capacity and as to action in another capacity while holding office. The corporation is specifically authorized to enter into individual contracts with any or all of its directors, officers, employees or agents respecting indemnification and advances, to the fullest extent not prohibited by the DGCL or any other applicable law.

(f) **Survival of Rights.** The rights conferred on any person by this Bylaw shall continue as to a person who has ceased to be a director, officer, employee or other agent and shall inure to the benefit of the heirs, executors and administrators of such a person.

(g) **Insurance.** To the fullest extent permitted by the DGCL, or any other applicable law, the corporation, upon approval by the Board of Directors, may purchase insurance on behalf of any person required or permitted to be indemnified pursuant to this Bylaw.

(h) **Amendments.** Any repeal or modification of this Bylaw shall only be prospective and shall not affect the rights under this Bylaw in effect at the time of the alleged occurrence of any action or omission to act that is the cause of any proceeding against any agent of the corporation.

(i) **Saving Clause.** If this Bylaw or any portion hereof shall be invalidated on any ground by any court of competent jurisdiction, then the corporation shall nevertheless indemnify each director and officer to the full extent not prohibited by any applicable portion of this Bylaw that shall not have been invalidated, or by any other applicable law. If this Section 43 shall be invalid due to the application of the indemnification provisions of another jurisdiction, then the corporation shall indemnify each director and officer to the full extent under applicable law.

(j) **Certain Definitions.** For the purposes of this Bylaw, the following definitions shall apply:

(1) The term “**proceeding**” shall be broadly construed and shall include, without limitation, the investigation, preparation, prosecution, defense, settlement,

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arbitration and appeal of, and the giving of testimony in, any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative.

(2) The term “**expenses**” shall be broadly construed and shall include, without limitation, court costs, attorneys’ fees, witness fees, fines, amounts paid in settlement or judgment and any other costs and expenses of any nature or kind incurred in connection with any proceeding.

(3) The term the “**corporation**” shall include, in addition to the resulting corporation, any constituent corporation (including any constituent of a constituent) absorbed in a consolidation or merger which, if its separate existence had continued, would have had power and authority to indemnify its directors, officers, and employees or agents, so that any person who is or was a director, officer, employee or agent of such constituent corporation, or is or was serving at the request of such constituent corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, shall stand in the same position under the provisions of this Bylaw with respect to the resulting or surviving corporation as he would have with respect to such constituent corporation if its separate existence had continued.

(4) References to a “**director**,” “**executive officer**,” “**officer**,” “**employee**,” or “**agent**” of the corporation shall include, without limitation, situations where such person is serving at the request of the corporation as, respectively, a director, executive officer, officer, employee, trustee or agent of another corporation, partnership, joint venture, trust or other enterprise.

(5) References to “**other enterprises**” shall include employee benefit plans; references to “**fines**” shall include any excise taxes assessed on a person with respect to an employee benefit plan; and references to “**servicing at the request of the corporation**” shall include any service as a director, officer, employee or agent of the corporation which imposes duties on, or involves services by, such director, officer, employee, or agent with respect to an employee benefit plan, its participants, or beneficiaries; and a person who acted in good faith and in a manner he reasonably believed to be in the interest of the participants and beneficiaries of an employee benefit plan shall be deemed to have acted in a manner “**not opposed to the best interests of the corporation**” as referred to in this Bylaw.

## ARTICLE XII

### NOTICES

#### Section 44. Notices.

(a) **Notice to Stockholders.** Written notice to stockholders of stockholder meetings shall be given as provided in Section 7 herein. Without limiting the manner by which notice may otherwise be given effectively to stockholders under any agreement or contract with such stockholder, and except as otherwise required by law, written notice to stockholders for purposes other than stockholder meetings may be sent by United States mail or nationally recognized overnight courier, or by facsimile, telegraph or telex or by electronic mail or other electronic means.

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(b) **Notice to Directors.** Any notice required to be given to any director may be given by the method stated in subsection (a), or as provided for in Section 21 of these Bylaws. If such notice is not delivered personally, it shall be sent to such address as such director shall have filed in writing with the Secretary, or, in the absence of such filing, to the last known post office address of such director.

(c) **Affidavit of Mailing.** An affidavit of mailing, executed by a duly authorized and competent employee of the corporation or its transfer agent appointed with respect to the class of stock affected or other agent, specifying the name and address or the names and addresses of the stockholder or stockholders, or director or directors, to whom any such notice or notices was or were given, and the time and method of giving the same, shall in the absence of fraud, be prima facie evidence of the facts therein contained.

(d) **Methods of Notice.** It shall not be necessary that the same method of giving notice be employed in respect of all recipients of notice, but one permissible method may be employed in respect of any one or more, and any other permissible method or methods may be employed in respect of any other or others.

(e) **Notice to Person with Whom Communication Is Unlawful.** Whenever notice is required to be given, under any provision of law or of the Certificate of Incorporation or Bylaws of the corporation, to any person with whom communication is unlawful, the giving of such notice to such person shall not be required and there shall be no duty to apply to any governmental authority or agency for a license or permit to give such notice to such person. Any action or meeting which shall be taken or held without notice to any such person with whom communication is unlawful shall have the same force and effect as if such notice had been duly given. In the event that the action taken by the corporation is such as to require the filing of a certificate under any provision of the DGCL, the certificate shall state, if such is the fact and if notice is required, that notice was given to all persons entitled to receive notice except such persons with whom communication is unlawful.

(f) **Notice to Stockholders Sharing an Address.** Except as otherwise prohibited under DGCL, any notice given under the provisions of DGCL, the Certificate of Incorporation or the Bylaws shall be effective if given by a single written notice to stockholders who share an address if consented to by the stockholders at that address to whom such notice is given. Such consent shall have been deemed to have been given if such stockholder fails to object in writing to the corporation within 60 days of having been given notice by the corporation of its intention to send the single notice. Any consent shall be revocable by the stockholder by written notice to the corporation.

### ARTICLE XIII

#### AMENDMENTS

**Section 45. Amendments.** The Board of Directors is expressly empowered to adopt, amend or repeal Bylaws of the corporation; *provided, however*, that the Board of Directors does not have the power to decrease the corporation's indemnification obligations under Article XI. The stockholders shall also have power to adopt, amend or repeal the Bylaws of the corporation;

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*provided, however*, that, in addition to any vote of the holders of any class or series of stock of the corporation required by law or by the Certificate of Incorporation, the affirmative vote of the holders of at least a majority of the voting power of all of the then-outstanding shares of the capital stock of the corporation entitled to vote generally in the election of directors, voting together as a single class, shall be required to adopt, amend or repeal any provision of the Bylaws of the corporation.

### ARTICLE XIV

#### RIGHT OF FIRST REFUSAL

**Section 46. Right of First Refusal.** No stockholder shall sell, assign, pledge, or in any manner transfer any of the shares of common stock of the corporation or any right or interest therein, whether voluntarily or by operation of law, or by gift or otherwise, except by a transfer which meets the requirements hereinafter set forth in this bylaw:

(a) If the stockholder desires to sell or otherwise transfer any of his shares of stock, then the stockholder shall first give written notice thereof to the corporation. The notice shall name the proposed transferee and state the number of shares to be transferred, the proposed consideration, and all other terms and conditions of the proposed transfer.

(b) For thirty (30) days following receipt of such notice, the corporation shall have the option to purchase the shares specified in the notice at the price and upon the terms set forth in such notice; *provided, however*, that, with the consent of the stockholder, the corporation shall have the option to purchase a lesser portion of the shares specified in said notice at the price and upon the terms set forth therein. In the event of a gift, property settlement or other transfer in which the proposed transferee is not paying the full price for the shares, and that is not otherwise exempted from the provisions of this Section 46, the price shall be deemed to be the fair market value of the stock at such time as determined in good faith by the Board of Directors. In the event the corporation elects to purchase all of the shares or, with consent of the stockholder, a lesser portion of the shares, it shall give written notice to the transferring stockholder of its election and settlement for said shares shall be made as provided below in paragraph (d).

(c) The corporation may assign its rights hereunder.

(d) In the event the corporation and/or its assignee(s) elect to acquire any of the shares of the transferring stockholder as specified in said transferring stockholder's notice, the Secretary of the corporation shall so notify the transferring stockholder and settlement thereof shall be made in cash within thirty (30) days after the Secretary of the corporation receives said transferring stockholder's notice; *provided* that if the terms of payment set forth in said transferring stockholder's notice were other than cash against delivery, the corporation and/or its assignee(s) shall pay for said shares on the same terms and conditions set forth in said transferring stockholder's notice.

(e) In the event the corporation and/or its assignees(s) do not elect to acquire all of the shares specified in the transferring stockholder's notice, said transferring stockholder may, within the sixty-day period following the expiration of the option rights granted to the

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corporation and/or its assignees(s) herein, transfer the shares specified in said transferring stockholder's notice which were not acquired by the corporation and/or its assignees(s) as specified in said transferring stockholder's notice. All shares so sold by said transferring stockholder shall continue to be subject to the provisions of this bylaw in the same manner as before said transfer.

(f) Anything to the contrary contained herein notwithstanding, the following transactions shall be exempt from the provisions of this bylaw:

(1) A stockholder's transfer of any or all shares held either during such stockholder's lifetime or on death by will or intestacy to such stockholder's immediate family or to any custodian or trustee for the account of such stockholder or such stockholder's immediate family or to any limited partnership of which the stockholder, members of such stockholder's immediate family or any trust for the account of such stockholder or such stockholder's

immediate family will be the general or limited partner(s) of such partnership. “*Immediate family*” as used herein shall mean spouse, lineal descendant, father, mother, brother, or sister of the stockholder making such transfer.

- (2) A stockholder’s bona fide pledge or mortgage of any shares with a commercial lending institution, provided that any subsequent transfer of said shares by said institution shall be conducted in the manner set forth in this bylaw.
- (3) A stockholder’s transfer of any or all of such stockholder’s shares to the corporation or to any other stockholder of the corporation.
- (4) A stockholder’s transfer of any or all of such stockholder’s shares to a person who, at the time of such transfer, is an officer or director of the corporation.
- (5) A corporate stockholder’s transfer of any or all of its shares pursuant to and in accordance with the terms of any merger, consolidation, reclassification of shares or capital reorganization of the corporate stockholder, or pursuant to a sale of all or substantially all of the stock or assets of a corporate stockholder.
- (6) A corporate stockholder’s transfer of any or all of its shares to any or all of its stockholders.
- (7) A transfer by a stockholder which is a limited or general partnership to any or all of its partners or former partners.

In any such case, the transferee, assignee, or other recipient shall receive and hold such stock subject to the provisions of this bylaw, and there shall be no further transfer of such stock except in accord with this bylaw.

(g) The provisions of this bylaw may be waived with respect to any transfer either by the corporation, upon duly authorized action of its Board of Directors, or by the stockholders, upon the express written consent of the owners of a majority of the voting power of the corporation (excluding the votes represented by those shares to be transferred by the transferring stockholder). This bylaw may be amended or repealed either by a duly authorized

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action of the Board of Directors or by the stockholders, upon the express written consent of the owners of a majority of the voting power of the corporation. The right of first refusal in this bylaw shall be superseded by any contractual right of first refusal between a stockholder of the Company and the Company.

(h) Any sale or transfer, or purported sale or transfer, of securities of the corporation shall be null and void unless the terms, conditions, and provisions of this bylaw are strictly observed and followed.

(i) The foregoing right of first refusal shall terminate on either of the following dates, whichever shall first occur:

- (1) At any time on or after March, 2016 if the corporation is then subject to Section 2115(b) of the CGCL; or
- (2) Upon the date securities of the corporation are first offered to the public pursuant to a registration statement filed with, and declared effective by, the United States Securities and Exchange Commission under the Securities Act of 1933, as amended.

(j) The certificates representing shares of stock of the corporation shall bear on their face the following legend so long as the foregoing right of first refusal remains in effect:

“THE SHARES REPRESENTED BY THIS CERTIFICATE ARE SUBJECT TO A RIGHT OF FIRST REFUSAL OPTION IN FAVOR OF THE CORPORATION AND/OR ITS ASSIGNEE(S), AS PROVIDED IN THE BYLAWS OF THE CORPORATION.”

## ARTICLE XV

### LOANS TO OFFICERS

**Section 47. Loans to Officers.** Except as otherwise prohibited under applicable law, the corporation may lend money to, or guarantee any obligation of, or otherwise assist any officer or other employee of the corporation or of its subsidiaries, including any officer or employee who is a Director of the corporation or its subsidiaries, whenever, in the judgment of the Board of Directors, such loan, guarantee or assistance may reasonably be expected to benefit the corporation. The loan, guarantee or other assistance may be with or without interest and may be unsecured, or secured in such manner as the Board of Directors shall approve, including, without limitation, a pledge of shares of stock of the corporation. Nothing in these Bylaws shall be deemed to deny, limit or restrict the powers of guaranty or warranty of the corporation at common law or under any statute.

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## PROTEON THERAPEUTICS, INC.

## 2006 EQUITY INCENTIVE PLAN

ADOPTED : MARCH 24, 2006  
 APPROVED BY STOCKHOLDERS : MARCH 24, 2006  
 TERMINATION DATE: MARCH 23, 2016

## 1. PURPOSES.

(a) **Eligible Stock Award Recipients.** The persons eligible to receive Stock Awards are Employees, Directors and Consultants.

(b) **Available Stock Awards.** The purpose of the Plan is to provide a means by which eligible recipients of Stock Awards may be given an opportunity to benefit from increases in value of the Common Stock through the granting of the following Stock Awards: (i) Incentive Stock Options, (ii) Nonstatutory Stock Options, (iii) stock bonuses, (iv) rights to acquire restricted stock, (v) Stock Appreciation Rights and (vi) Phantom Stock Awards.

(c) **General Purpose.** The Company, by means of the Plan, seeks to retain the services of the group of persons eligible to receive Stock Awards, to secure and retain the services of new members of this group and to provide incentives for such persons to exert maximum efforts for the success of the Company and its Affiliates.

## 2. DEFINITIONS.

(a) **"Affiliate"** means any parent corporation or subsidiary corporation of the Company, whether now or hereafter existing, as those terms are defined in Sections 424(e) and (f), respectively, of the Code.

(b) **"Board"** means the Board of Directors of the Company.

(c) **"Capitalization Adjustment"** has the meaning ascribed to that term in Section 11(a).

(d) **"Change in Control"** means the occurrence, in a single transaction or in a series of related transactions, of any one or more of the following events:

(i) any Exchange Act Person becomes the Owner, directly or indirectly, of securities of the Company representing more than fifty percent (50%) of the combined voting power of the Company's then outstanding securities other than by virtue of a merger, consolidation or similar transaction;

(ii) there is consummated a merger, consolidation or similar transaction involving (directly or indirectly) the Company if, immediately after the consummation of such merger, consolidation or similar transaction, the stockholders of the Company immediately prior thereto do not Own, directly or indirectly, either (A) outstanding voting securities representing more than fifty percent (50%) of the combined outstanding voting power of the surviving Entity

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in such merger, consolidation or similar transaction or (B) more than fifty percent (50%) of the combined outstanding voting power of the parent of the surviving Entity in such merger, consolidation or similar transaction;

(iii) the stockholders of the Company approve or the Board approves a plan of complete dissolution or liquidation of the Company, or a complete dissolution or liquidation of the Company shall otherwise occur; or

(iv) there is consummated a sale, lease, license or other disposition of all or substantially all of the consolidated assets of the Company and its Subsidiaries, other than a sale, lease, license or other disposition of all or substantially all of the consolidated assets of the Company and its Subsidiaries to an Entity, more than fifty percent (50%) of the combined voting power of the voting securities of which are Owned by stockholders of the Company in substantially the same proportion as their Ownership of the Company immediately prior to such sale, lease, license or other disposition.

The term Change in Control shall not include a sale of assets, merger or other transaction effected exclusively for the purpose of changing the domicile of the Company, or for primarily fundraising purposes.

Notwithstanding the foregoing or any other provision of this Plan, the definition of Change in Control (or any analogous term) in an individual written agreement between the Company or any Affiliate and the Participant shall supersede the foregoing definition with respect to Stock Awards subject to such agreement (it being understood, however, that if no definition of Change in Control or any analogous term is set forth in such an individual written agreement, the foregoing definition shall apply).

(e) **"Code"** means the Internal Revenue Code of 1986, as amended.

(f) **"Committee"** means a committee of one or more members of the Board appointed by the Board in accordance with Section 3(c).

(g) **"Common Stock"** means the common stock of the Company.

(h) **"Company"** means Proteon Therapeutics, Inc., a Delaware corporation.

(i) **"Consultant"** means any person, including an advisor, (i) engaged by the Company or an Affiliate to render consulting or advisory services and who is compensated for such services or (ii) serving as a member of the Board of Directors of an Affiliate and who is compensated for such services. However, the term "Consultant" shall not include Directors who are not compensated by the Company for their services as Directors, and the payment of a director's fee by the Company for services as a Director shall not cause a Director to be considered a "Consultant" for purposes of the Plan.

(j) **“Continuous Service”** means that the Participant’s service with the Company or an Affiliate, whether as an Employee, Director or Consultant, is not interrupted or terminated. A change in the capacity in which the Participant renders service to the Company or an Affiliate as an Employee, Consultant or Director or a change in the entity for which the Participant renders

such service, provided that there is no interruption or termination of the Participant’s service with the Company or an Affiliate, shall not terminate a Participant’s Continuous Service. For example, a change in status from an employee of the Company to a consultant to an Affiliate or to a Director shall not constitute an interruption of Continuous Service. The Board, in its sole discretion, may determine whether Continuous Service shall be considered interrupted in the case of any leave of absence approved by that party, including sick leave, military leave or any other personal leave. Notwithstanding the foregoing, a leave of absence shall be treated as Continuous Service for purposes of vesting in a Stock Award only to such extent as may be provided in the Company’s leave of absence policy or in the written terms of the Participant’s leave of absence.

(k) **“Corporate Transaction”** means the occurrence, in a single transaction or in a series of related transactions, of any one or more of the following events:

- (i) a sale or other disposition of all or substantially all, as determined by the Board in its discretion, of the consolidated assets of the Company and its Subsidiaries;
- (ii) a sale or other disposition of at least ninety percent (90%) of the outstanding securities of the Company;
- (iii) a merger, consolidation or similar transaction following which the Company is not the surviving corporation; or
- (iv) a merger, consolidation or similar transaction following which the Company is the surviving corporation but the shares of Common Stock outstanding immediately preceding the merger, consolidation or similar transaction are converted or exchanged by virtue of the merger, consolidation or similar transaction into other property, whether in the form of securities, cash or otherwise.

(l) **“Director”** means a member of the Board.

(m) **“Disability”** means the inability of a person, in the opinion of a qualified physician acceptable to the Company, to perform the major duties of that person’s position with the Company or an Affiliate because of the sickness or injury of the person.

(n) **“Employee”** means any person employed by the Company or an Affiliate. Service as a Director or payment of a director’s fee by the Company for such service or for service as a member of the Board of Directors of an Affiliate shall not be sufficient to constitute “employment” by the Company or an Affiliate.

**“Entity”** means a corporation, partnership or other entity.

(o) **“Exchange Act”** means the Securities Exchange Act of 1934, as amended.

(p) **“Exchange Act Person”** means any natural person, Entity or “group” (within the meaning of Section 13(d) or 14(d) of the Exchange Act), except that “Exchange Act Person” shall not include (A) the Company or any Subsidiary of the Company, (B) any employee benefit plan of the Company or any Subsidiary of the Company or any trustee or other fiduciary holding

securities under an employee benefit plan of the Company or any Subsidiary of the Company, (C) an underwriter temporarily holding securities pursuant to an offering of such securities, or (D) an Entity Owned, directly or indirectly, by the stockholders of the Company in substantially the same proportions as their Ownership of stock of the Company.

(q) **“Fair Market Value”** means, as of any date, the value of the Common Stock determined in good faith by the Board, and if required by applicable law, in a manner consistent with Section 260.140.50 of Title 10 of the California Code of Regulations.

(r) **“Incentive Stock Option”** means an Option intended to qualify as an incentive stock option within the meaning of Section 422 of the Code and the regulations promulgated thereunder.

(s) **“Nonstatutory Stock Option”** means an Option not intended to qualify as an Incentive Stock Option.

(t) **“Officer”** means any person designated by the Company as an officer.

(u) **“Option”** means an Incentive Stock Option or a Nonstatutory Stock Option granted pursuant to the Plan.

(v) **“Option Agreement”** means a written agreement between the Company and an Optionholder evidencing the terms and conditions of an individual Option grant. Each Option Agreement shall be subject to the terms and conditions of the Plan.

(w) **“Optionholder”** means a person to whom an Option is granted pursuant to the Plan or, if applicable, such other person who holds an outstanding Option.

(x) **“Own,” “Owned,” “Owner,” “Ownership”** A person or Entity shall be deemed to “Own,” to have “Owned,” to be the “Owner” of, or to have acquired “Ownership” of securities if such person or Entity, directly or indirectly, through any contract, arrangement, understanding, relationship or otherwise, has or shares voting power, which includes the power to vote or to direct the voting, with respect to such securities.

(y) **“Participant”** means a person to whom a Stock Award is granted pursuant to the Plan or, if applicable, such other person who holds an outstanding Stock Award.



(z) **“Phantom Stock Award”** means an award of a specified number of units of value granted under the Plan, which, when redeemed, shall be a right to receive cash from the Company in an amount equal to the Fair Market Value of the Common Stock as determined in accordance with this Plan.

(aa) **“Plan”** means this Proteon Therapeutics, Inc. 2006 Equity Incentive Plan.

(bb) **“Restricted Stock Award”** means an award of shares of Common Stock that is granted pursuant to the terms and conditions of Section 7(b).

(cc) **“Securities Act”** means the Securities Act of 1933, as amended.

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(dd) **“Stock Appreciation Right” or “SAR”** means a single unit of value granted under the Plan, which, when redeemed, shall be a right to receive cash from the Company in an amount equal to the Fair Market Value of the Common Stock, as determined in accordance with this Plan, minus the exercise price, if any, of the SAR.

(ee) **“Stock Award”** means any right granted under the Plan, including an Option, a stock bonus and a right to acquire restricted stock.

(ff) **“Stock Award Agreement”** means a written agreement between the Company and a holder of a Stock Award evidencing the terms and conditions of an individual Stock Award grant. Each Stock Award Agreement shall be subject to the terms and conditions of the Plan.

(gg) **“Subsidiary”** means, with respect to the Company, (i) any corporation of which more than fifty percent (50%) of the outstanding capital stock having ordinary voting power to elect a majority of the board of directors of such corporation (irrespective of whether, at the time, stock of any other class or classes of such corporation shall have or might have voting power by reason of the happening of any contingency) is at the time, directly or indirectly, Owned by the Company, and (ii) any partnership in which the Company has a direct or indirect interest (whether in the form of voting or participation in profits or capital contribution) of more than fifty percent (50%).

(hh) **“Ten Percent Stockholder”** means a person who Owns (or is deemed to Own pursuant to Section 424(d) of the Code) stock possessing more than ten percent (10%) of the total combined voting power of all classes of stock of the Company or of any of its Affiliates.

### 3. ADMINISTRATION.

(a) **Administration by Board.** The Board shall administer the Plan unless and until the Board delegates administration to a Committee, as provided in Section 3(c).

(b) **Powers of Board.** The Board shall have the power, subject to, and within the limitations of, the express provisions of the Plan:

(i) To determine from time to time which of the persons eligible under the Plan shall be granted Stock Awards; when and how each Stock Award shall be granted; what type or combination of types of Stock Award shall be granted; the provisions of each Stock Award granted (which need not be identical), including the time or times when a person shall be permitted to receive Common Stock pursuant to a Stock Award; and the number of shares of Common Stock, or units of value for Stock Appreciation Rights or Phantom Stock Awards, with respect to which a Stock Award shall be granted to each such person.

(ii) To construe and interpret the Plan and Stock Awards granted under it, and to establish, amend and revoke rules and regulations for its administration. The Board, in the exercise of this power, may correct any defect, omission or inconsistency in the Plan or in any Stock Award Agreement, in a manner and to the extent it shall deem necessary or expedient to make the Plan fully effective.

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(iii) To effect, at any time and from time to time, with the consent of any adversely affected Optionholder, (1) the reduction of the exercise price of any outstanding Option under the Plan, (2) the cancellation of any outstanding Option under the Plan and the grant in substitution therefor of (A) a new Option under the Plan or another equity plan of the Company covering the same or a different number of shares of Common Stock, (B) a Restricted Stock Award (including a stock bonus), (C) a Stock Appreciation Right, (D) cash (E) Phantom Stock Awards and/or (F) other valuable consideration (as determined by the Board, in its sole discretion), or (3) any other action that is treated as a repricing under generally accepted accounting principles.

(iv) To amend the Plan or a Stock Award as provided in Section 12.

(v) To terminate or suspend the Plan as provided in Section 13.

(vi) Generally, to exercise such powers and to perform such acts as the Board deems necessary or expedient to promote the best interests of the Company and that are not in conflict with the provisions of the Plan.

(c) **Delegation to Committee.** The Board may delegate administration of the Plan to a Committee or Committees of three (3) or more members of the Board, and the term “Committee” shall apply to any person or persons to whom such authority has been delegated. If administration is delegated to a Committee, the Committee shall have, in connection with the administration of the Plan, the powers theretofore possessed by the Board, including the power to delegate to a subcommittee any of the administrative powers the Committee is authorized to exercise (and references in this Plan to the Board shall thereafter be to the Committee or subcommittee), subject, however, to such resolutions, not inconsistent with the provisions of the Plan, as may be adopted from time to time by the Board. The Board may abolish the Committee at any time and revert in the Board the administration of the Plan.

(d) **Delegation to an Officer.** The Board may delegate to one or more Officers of the Company the authority to do one or both of the following: (i) designate Officers and Employees of the Company or any of its Subsidiaries to be recipients of Stock Awards and (ii) determine the number of shares of Common Stock to be subject to such Stock Awards granted to such Officers and Employees of the Company; *provided, however*, that the Board resolutions regarding such delegation shall specify the total number of shares of Common Stock that may be subject to the Stock Awards granted by such Officer and that such Officer may not grant a Stock Award to himself or herself. Notwithstanding the foregoing, the Board may not delegate authority to an Officer to determine the Fair Market Value of the Common Stock.

(e) **Effect of Board's Decision.** All determinations, interpretations and constructions made by the Board in good faith shall not be subject to review by any person and shall be final, binding and conclusive on all persons.

#### 4. SHARES SUBJECT TO THE PLAN.

(a) **Share Reserve.** Subject to the provisions of Section 11(a) relating to Capitalization Adjustments, the Common Stock and units of value for Stock Appreciation Rights

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or Phantom Stock Awards that may be issued pursuant to Stock Awards shall not exceed in the aggregate three million (3,000,000)\* shares of Common Stock.

(b) **Reversion of Shares to the Share Reserve.** If any Stock Award shall for any reason expire or otherwise terminate, in whole or in part, without having been exercised or redeemed in full, the shares of Common Stock not acquired under such Stock Award shall revert to and again become available for issuance under the Plan.

(c) **Source of Shares.** The shares of Common Stock subject to the Plan may be unissued shares or reacquired shares, bought on the market or otherwise.

(d) **Share Reserve Limitation.** To the extent that it may be required by Section 260.140.45 of Title 10 of the California Code of Regulations, the total number of shares of Common Stock issuable upon exercise of all outstanding Options and the total number of shares of Common Stock provided for under any stock bonus or similar plan of the Company shall not exceed the applicable percentage as calculated in accordance with the conditions and exclusions of Section 260.140.45 of Title 10 of the California Code of Regulations, based on the shares of Common Stock of the Company that are outstanding at the time the calculation is made.

#### 5. ELIGIBILITY.

(a) **Eligibility for Specific Stock Awards.** Incentive Stock Options may be granted only to Employees. Stock Awards other than Incentive Stock Options may be granted to Employees, Directors and Consultants.

(b) **Ten Percent Stockholders.**

(i) A Ten Percent Stockholder shall not be granted an Incentive Stock Option unless the exercise price of such Option is at least one hundred ten percent (110%) of the Fair Market Value of the Common Stock on the date of grant and the Option is not exercisable after the expiration of five (5) years from the date of grant.

(ii) A Ten Percent Stockholder shall not be granted a Nonstatutory Stock Option unless the exercise price of such Option is at least (i) one hundred ten percent (110%) of the Fair Market Value of the Common Stock on the date of grant or (ii) such lower percentage of the Fair Market Value of the Common Stock on the date of grant as is permitted by Section 260.140.41 of Title 10 of the California Code of Regulations at the time of the grant of the Option, if applicable.

(iii) A Ten Percent Stockholder shall not be granted a restricted stock award unless the purchase price of the restricted stock is at least (i) one hundred percent (100%) of the Fair Market Value of the Common Stock on the date of grant or (ii) such lower percentage of the Fair Market Value of the Common Stock on the date of grant as is permitted by Section 260.140.42 of Title 10 of the California Code of Regulations at the time of the grant of the restricted stock award, if applicable.

(c) **Consultants.** A Consultant shall not be eligible for the grant of a Stock Award if, at the time of grant, either the offer or the sale of the Company's securities to such Consultant is

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not exempt under Rule 701 of the Securities Act ("Rule 701") because of the nature of the services that the Consultant is providing to the Company, because the Consultant is not a natural person, or because of some other provision of Rule 701, unless the Company determines that such grant need not comply with the requirements of Rule 701 and will satisfy another exemption under the Securities Act as well as comply with the securities laws of all other relevant jurisdictions, if applicable.

#### 6. OPTION PROVISIONS.

Each Option shall be in such form and shall contain such terms and conditions as the Board shall deem appropriate. All Options shall be separately designated Incentive Stock Options or Nonstatutory Stock Options at the time of grant, and, if certificates are issued, a separate certificate or certificates shall be issued for shares of Common Stock purchased on exercise of each type of Option. The provisions of separate Options need not be identical, but each Option shall include (through incorporation of provisions hereof by reference in the Option or otherwise) the substance of each of the following provisions:

(a) **Term.** Subject to the provisions of Section 5(b) regarding Ten Percent Stockholders, no Option shall be exercisable after the expiration of ten (10) years from the date it was granted.

(b) **Exercise Price of an Incentive Stock Option.** Subject to the provisions of Section 5(b) regarding Ten Percent Stockholders, the exercise price of each Incentive Stock Option shall be not less than one hundred percent (100%) of the Fair Market Value of the Common Stock subject to the Option on the date the Option is granted. Notwithstanding the foregoing, an Incentive Stock Option may be granted with an exercise price lower than that set forth in the preceding sentence if such Option is granted pursuant to an assumption or substitution for another option in a manner satisfying the provisions of Section 424(a) of the Code.

(c) **Exercise Price of a Nonstatutory Stock Option.** Subject to the provisions of Section 5(b) regarding Ten Percent Stockholders, the exercise price of each Nonstatutory Stock Option shall be not less than eighty-five percent (85%) of the Fair Market Value of the Common Stock subject to the Option on the date the Option is granted. Notwithstanding the foregoing, a Nonstatutory Stock Option may be granted with an exercise price lower than that set forth in the preceding sentence if such Option is granted pursuant to an assumption or substitution for another option in a manner satisfying the provisions of Section 424(a) of the Code.

(d) **Consideration.** The purchase price of Common Stock acquired pursuant to an Option shall be paid, to the extent permitted by applicable statutes and regulations, either (i) in cash at the time the Option is exercised or (ii) at the discretion of the Board at the time of the grant of the Option (or subsequently in the case of a Nonstatutory Stock Option) (1) by delivery to the Company of other Common Stock, (2) according to a deferred payment or other similar arrangement with the Optionholder or (3) in any other form of legal consideration that may be acceptable to the Board. Unless otherwise specifically provided in the Option, the purchase price of Common Stock acquired pursuant to an Option that is paid by delivery to the Company of other Common Stock acquired, directly or indirectly from the Company, shall be paid only by

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shares of the Common Stock of the Company that have been held for more than six (6) months (or such longer or shorter period of time required to avoid a charge to earnings for financial accounting purposes). At any time that the Company is incorporated in Delaware, payment of the Common Stock's "par value," as defined in the Delaware General Corporation Law, shall not be made by deferred payment.

In the case of any deferred payment arrangement, interest shall be compounded at least annually and shall be charged at the minimum rate of interest necessary to avoid (1) the treatment as interest, under any applicable provisions of the Code, of any amounts other than amounts stated to be interest under the deferred payment arrangement and (2) the treatment of the Option as a variable award for financial accounting purposes.

(e) **Transferability of an Incentive Stock Option.** An Incentive Stock Option shall not be transferable except by will or by the laws of descent and distribution and shall be exercisable during the lifetime of the Optionholder only by the Optionholder. Notwithstanding the foregoing, the Optionholder may, by delivering written notice to the Company, in a form satisfactory to the Company, designate a third party who, in the event of the death of the Optionholder, shall thereafter be entitled to exercise the Option.

(f) **Transferability of a Nonstatutory Stock Option.** A Nonstatutory Stock Option shall not be transferable except by will or by the laws of descent and distribution and, to the extent provided in the Option Agreement, to such further extent as permitted by Section 260.140.41(d) of Title 10 of the California Code of Regulations, if applicable at the time of the grant of the Option, and shall be exercisable during the lifetime of the Optionholder only by the Optionholder. If the Nonstatutory Stock Option does not provide for transferability, then the Nonstatutory Stock Option shall not be transferable except by will or by the laws of descent and distribution and shall be exercisable during the lifetime of the Optionholder only by the Optionholder. Notwithstanding the foregoing, the Optionholder may, by delivering written notice to the Company, in a form satisfactory to the Company, designate a third party who, in the event of the death of the Optionholder, shall thereafter be entitled to exercise the Option.

(g) **Vesting Generally.** The total number of shares of Common Stock subject to an Option may, but need not, vest and therefore become exercisable in periodic installments that may, but need not, be equal. The Option may be subject to such other terms and conditions on the time or times when it may be exercised (which may be based on performance or other criteria) as the Board may deem appropriate. The vesting provisions of individual Options may vary. The provisions of this Section 6(g) are subject to any Option provisions governing the minimum number of shares of Common Stock as to which an Option may be exercised.

(h) **Minimum Vesting.** Notwithstanding the foregoing Section 6(g), to the extent that the following restrictions on vesting are required by Section 260.140.41(f) of Title 10 of the California Code of Regulations at the time of the grant of the Option, then:

(i) Options granted to an Employee who is not an Officer, Director or Consultant shall provide for vesting of the total number of shares of Common Stock at a rate of at least twenty percent (20%) per year over five (5) years from the date the Option was granted, subject to reasonable conditions such as continued employment; and

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(ii) Options granted to Officers, Directors or Consultants may be made fully exercisable, subject to reasonable conditions such as continued employment, at any time or during any period established by the Company.

(i) **Termination of Continuous Service.** In the event that an Optionholder's Continuous Service terminates (other than upon the Optionholder's death or Disability), the Optionholder may exercise his or her Option (to the extent that the Optionholder was entitled to exercise such Option as of the date of termination) but only within such period of time ending on the earlier of (i) the date three (3) months following the termination of the Optionholder's Continuous Service (or such longer or shorter period specified in the Option Agreement), or (ii) the expiration of the term of the Option as set forth in the Option Agreement. If, after termination, the Optionholder does not exercise his or her Option within the time specified in the Option Agreement, the Option shall terminate.

(j) **Extension of Termination Date.** An Optionholder's Option Agreement may also provide that if the exercise of the Option following the termination of the Optionholder's Continuous Service (other than upon the Optionholder's death or Disability) would be prohibited at any time solely because the issuance of shares of Common Stock would violate the registration requirements under the Securities Act, then the Option shall terminate on the earlier of (i) the expiration of the term of the Option set forth in Section 6(a) or (ii) the expiration of a period of three (3) months after the termination of the Optionholder's Continuous Service during which the exercise of the Option would not be in violation of such registration requirements.

(k) **Disability of Optionholder.** In the event that an Optionholder's Continuous Service terminates as a result of the Optionholder's Disability, the Optionholder may exercise his or her Option (to the extent that the Optionholder was entitled to exercise such Option as of the date of termination), but only within such period of time ending on the earlier of (i) the date twelve (12) months following such termination (or such longer or shorter period specified in the Option Agreement, which period shall not be less than six (6) months) or (ii) the expiration of the term of the Option as set forth in the Option Agreement. If, after termination, the Optionholder does not exercise his or her Option within the time specified herein, the Option shall terminate.

(l) **Death of Optionholder.** In the event that (i) an Optionholder's Continuous Service terminates as a result of the Optionholder's death or (ii) the Optionholder dies within the period (if any) specified in the Option Agreement after the termination of the Optionholder's Continuous Service for a reason other than death, then the Option may be exercised (to the extent the Optionholder was entitled to exercise such Option as of the date of death) by the Optionholder's estate, by a person who acquired the right to exercise the Option by bequest or inheritance or by a person designated to exercise the option upon the Optionholder's death pursuant to Section 6(e) or 6(f), but only within the period ending on the earlier of (1) the date eighteen (18) months following the date of death (or such longer or shorter period specified in the Option Agreement, which period shall not be less than six (6) months) or (2) the expiration of the term of such Option as set forth in the Option Agreement. If, after death, the Option is not exercised within the time specified herein, the Option shall terminate.

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**(m) Early Exercise.** The Option may, but need not, include a provision whereby the Optionholder may elect at any time before the Optionholder's Continuous Service terminates to exercise the Option as to any part or all of the shares of Common Stock subject to the Option prior to the full vesting of the Option. Subject to the "Repurchase Limitation" in Section 10(h), any unvested shares of Common Stock so purchased may be subject to a repurchase option in favor of the Company or to any other restriction the Board determines to be appropriate. Provided that the "Repurchase Limitation" in Section 10(h) is not violated, the Company will not exercise its repurchase option until at least six (6) months (or such longer or shorter period of time required to avoid a charge to earnings for financial accounting purposes) have elapsed following exercise of the Option unless the Board otherwise specifically provides in the Option.

**(n) Right of Repurchase.** Subject to the "Repurchase Limitation" in Section 10(h), the Option may, but need not, include a provision whereby the Company may elect to repurchase all or any part of the vested shares of Common Stock acquired by the Optionholder pursuant to the exercise of the Option. Provided that the "Repurchase Limitation" in Section 10(h) is not violated, the Company will not exercise its repurchase option until at least six (6) months (or such longer or shorter period of time required to avoid a charge to earnings for financial accounting purposes) have elapsed following exercise of the Option unless otherwise specifically provided in the Option.

**(o) Right of First Refusal.** The Option may, but need not, include a provision whereby the Company may elect to exercise a right of first refusal following receipt of notice from the Optionholder of the intent to transfer all or any part of the shares of Common Stock received upon the exercise of the Option. Except as expressly provided in this Section 6(o) or in the Stock Award Agreement for the Option, such right of first refusal shall otherwise comply with any applicable provisions of the Bylaws of the Company. The Company will not exercise its right of first refusal until at least six (6) months (or such longer or shorter period of time required to avoid a charge to earnings for financial accounting purposes) have elapsed following the exercise of the Option unless otherwise specifically provided in the Option.

## 7. PROVISIONS OF STOCK AWARDS OTHER THAN OPTIONS.

**(a) Stock Bonus Awards.** Each stock bonus agreement shall be in such form and shall contain such terms and conditions as the Board shall deem appropriate. The terms and conditions of stock bonus agreements may change from time to time, and the terms and conditions of separate stock bonus agreements need not be identical, but each stock bonus agreement shall include (through incorporation of provisions hereof by reference in the agreement or otherwise) the substance of each of the following provisions:

**(i) Consideration.** A stock bonus may be awarded in consideration for past services actually rendered to the Company or an Affiliate for its benefit.

**(ii) Vesting.** Subject to the "Repurchase Limitation" in Section 10(h), shares of Common Stock awarded under the stock bonus agreement may, but need not, be subject to a share repurchase option in favor of the Company in accordance with a vesting schedule to be determined by the Board.

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**(iii) Termination of Participant's Continuous Service.** Subject to the "Repurchase Limitation" in Section 10(h), in the event that a Participant's Continuous Service terminates, the Company may reacquire any or all of the shares of Common Stock held by the Participant that have not vested as of the date of termination under the terms of the stock bonus agreement. Provided that the "Repurchase Limitation" in Section 10(h) is not violated, the Company will not exercise its repurchase option until at least six (6) months (or such longer or shorter period of time required to avoid a charge to earnings for financial accounting purposes) have elapsed following receipt of the stock bonus unless otherwise specifically provided in the stock bonus agreement.

**(iv) Transferability.** Rights to acquire shares of Common Stock under the stock bonus agreement shall not be transferable except by will or by the laws of descent and distribution and shall be exercisable during the lifetime of the Participant only by the Participant.

**(b) Restricted Stock Awards.** Each restricted stock purchase agreement shall be in such form and shall contain such terms and conditions as the Board shall deem appropriate. The terms and conditions of the restricted stock purchase agreements may change from time to time, and the terms and conditions of separate restricted stock purchase agreements need not be identical, but each restricted stock purchase agreement shall include (through incorporation of provisions hereof by reference in the agreement or otherwise) the substance of each of the following provisions:

**(i) Purchase Price.** Subject to the provisions of Section 5(b) regarding Ten Percent Stockholders, the purchase price of restricted stock awards shall not be less than eighty-five percent (85%) of the Common Stock's Fair Market Value on the date such award is made or at the time the purchase is consummated.

**(ii) Consideration.** The purchase price of Common Stock acquired pursuant to the restricted stock purchase agreement shall be paid either: (i) in cash at the time of purchase; (ii) at the discretion of the Board, according to a deferred payment or other similar arrangement with the Participant; or (iii) in any other form of legal consideration that may be acceptable to the Board in its discretion; *provided, however*, that at any time that the Company is incorporated in Delaware, then payment of the Common Stock's "par value," as defined in the Delaware General Corporation Law, shall not be made by deferred payment.

**(iii) Vesting.** Subject to the "Repurchase Limitation" in Section 10(h), shares of Common Stock acquired under the restricted stock purchase agreement may, but need not, be subject to a share repurchase option in favor of the Company in accordance with a vesting schedule to be determined by the Board.

**(iv) Termination of Participant's Continuous Service.** Subject to the "Repurchase Limitation" in Section 10(h), in the event that a Participant's Continuous Service terminates, the Company may repurchase or otherwise reacquire any or all of the shares of Common Stock held by the Participant that have not vested as of the date of termination under the terms of the restricted stock purchase agreement. Provided that the "Repurchase Limitation" in Section 10(h) is not violated, the Company will not exercise its repurchase option until at least six (6) months (or such longer or shorter period of time required to avoid a charge to earnings for

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financial accounting purposes) have elapsed following the purchase of the restricted stock unless otherwise specifically provided in the restricted stock purchase agreement.

(v) **Transferability.** Rights to acquire shares of Common Stock under the restricted stock purchase agreement shall not be transferable except by will or by the laws of descent and distribution and shall be exercisable during the lifetime of the Participant only by the Participant.

(c) **Stock Appreciation Rights and Phantom Stock Awards.** Each SAR and Phantom Stock Award agreement shall be in such form and shall contain such terms and conditions as the Board shall deem appropriate. The terms and conditions of SAR and Phantom Stock Award agreements may change from time to time, and the terms and conditions of separate SAR and Phantom Stock Award agreements need not be identical, but each SAR and Phantom Stock Award agreement shall include (through incorporation of provisions hereof by reference in the agreement or otherwise) the substance of each of the following provisions:

(i) **Grants.** SARs and Phantom Stock Awards granted to a Participant shall be credited to a bookkeeping account to be maintained for such Participant. A Participant may be granted more than one SAR or Phantom Stock Award under the Plan, and such Participant shall be notified of each such grant in writing within thirty (30) days of the date of grant, or within such other time period as the Board shall determine is appropriate.

(ii) **Term.** Each SAR and Phantom Stock Award granted pursuant to the Plan shall have a term of ten (10) years. A SAR or Phantom Stock Award not redeemed prior to the payment shall be made to the Participant holding such SAR or Phantom Stock Award in accordance with this Section 7(c).

(iii) **Vesting and Forfeiture.** SARs and the units subject to each Phantom Stock Award shall become vested and redeemable in periodic installments that may, but need not, be equal. The SAR or Phantom Stock Award may be subject to such other terms and conditions on the time or times when it may be redeemed (which may be based on performance or other criteria) as the Board may deem appropriate. The vesting provisions of individual SARs and Phantom Stock Awards may vary.

A Participant's SARs or Phantom Stock Awards shall continue to vest until either (i) the Participant's Continuous Service terminates for any reason, or (ii) all SARs or units subject to the Phantom Stock Award under the Participant's grant become fully vested. Only SARs and units subject to the Phantom Stock Awards that are vested may be redeemed.

If a Participant's Continuous Service terminates for any reason before all SARs or units subject to a Phantom Stock Award held by such Participant have vested, the portion of those SARs or Phantom Stock Awards that has not vested as of the date of such termination of Continuous Service shall be forfeited and canceled as of such date. Such Participant's SARs and vested units subject to the Phantom Stock Award that have vested automatically shall be redeemed on the date of his or her termination, and the Participant shall receive a cash payment for such automatically redeemed vested SARs and Phantom Stock Awards in accordance with Section 7(c)(iv).

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If a Participant's Continuous Service with the Company is interrupted for a period of three (3) months or more in a calendar year for any reason, including such Participant's sick leave, maternity leave, military leave, or other leave of absence approved by the Company, before all SARs or units subject to a Phantom Stock Award held by such Participant have vested, then upon the occurrence of such interruption, further vesting of the SARs and Phantom Stock Awards shall cease until the Participant resumes Continuous Service. The unvested SARs and Phantom Stock Awards thereafter shall vest on the basis set forth in the Participant's SAR or Phantom Stock Award agreement, with no vesting credit given for the period during which the vesting ceased.

Notwithstanding the foregoing, the Board shall have the power to accelerate the time of vesting for any Participant or Participants under this Section 7(c), including in the event of a Change in Control or a Participant's termination of Continuous Service.

(iv) **Redemption.** SARs and Phantom Stock Awards shall entitle the holder to receive a cash payment from the Company upon redemption in an amount equal to the Fair Market Value per share of the Common Stock (or such other value per share as may be set forth in the SAR or Phantom Stock Award agreement), multiplied by the number of SARs or units as to which the Phantom Stock Award is redeemed, less the applicable exercise price, if any, and applicable withholding taxes and authorized payroll deductions. Such payments shall be made as soon as reasonably practicable following the redemption of a SAR or Phantom Stock Award. Notwithstanding the foregoing a SAR or Phantom Stock Award agreement may provide that the Company may, in its sole discretion, make payment following a redemption of a SAR or Phantom Stock Award pursuant to a deferred payment schedule. Such deferred payment schedule shall provide that the Company shall pay the Participant the payment due with respect to the redemption within a period certain not to exceed two years from the date of the redemption. Payments made pursuant to a deferred payment schedule will include an interest payment by the Company in an amount equal to the mid-term Applicable Federal Rate established by the Internal Revenue Service, compounded annually, on the unpaid balance of the payment over the actual term of the payment.

At the time of the redemption of a SAR or Phantom Stock Award, the Participant shall execute such additional documents as the Company may then require in order to administer properly the terms of the grant and redemption.

(v) **Transferability.** SARs and Phantom Stock Awards shall not be transferable or assignable in any manner by a Participant. During the lifetime of a Participant, vested SARs and units subject to Phantom Stock Awards held by such Participant shall be redeemed only by such Participant or his or her guardian or legal representative. In the case of the death of a Participant who holds vested SARs or units subject to Phantom Stock Awards, such vested SARs or units subject to Phantom Stock Awards automatically shall be redeemed as of the Participant's date of death, and payment shall be made to such Participant's designated beneficiary or, in the absence of designation, to such Participant's beneficiary by will or by the laws of descent and distribution upon sufficient legal proof of entitlement, in accordance with Section 7(c)(iv) of the Plan.

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(vi) **Funding.** SARs and Phantom Stock Awards shall not be funded, the Company shall not be required to segregate any funds representing the value of SARs or Phantom Stock Awards granted to Participants, and nothing in the Plan shall be construed as providing for such segregation. A Participant's rights to amounts received upon the redemption of SARs or Phantom Stock Awards under the Plan shall be those of an unsecured general creditor of the Company. The liability for payment upon the redemption of a SAR or Phantom Stock Award shall be a liability of the Company alone and shall not be a liability of any officer, director, shareholder or affiliate of the Company.

## 8. COVENANTS OF THE COMPANY.

(a) **Availability of Shares.** During the terms of the Stock Awards, the Company shall keep available at all times the number of shares of Common Stock required to satisfy such Stock Awards.

(b) **Securities Law Compliance.** The Company shall seek to obtain from each regulatory commission or agency having jurisdiction over the Plan such authority as may be required to grant Stock Awards and to issue and sell shares of Common Stock upon exercise of the Stock Awards; *provided, however*, that this undertaking shall not require the Company to register under the Securities Act the Plan, any Stock Award or any Common Stock issued or issuable pursuant to any such Stock Award. If, after reasonable efforts, the Company is unable to obtain from any such regulatory commission or agency the authority which counsel for the Company deems necessary for the lawful issuance and sale of Common Stock under the Plan, the Company shall be relieved from any liability for failure to issue and sell Common Stock upon exercise of such Stock Awards unless and until such authority is obtained.

## 9. USE OF PROCEEDS FROM STOCK

Proceeds from the sale of Common Stock pursuant to Stock Awards shall constitute general funds of the Company.

## 10. MISCELLANEOUS.

(a) **Acceleration of Exercisability or Redemption and Vesting.** The Board shall have the power to accelerate the time at which a Stock Award may first be exercised or redeemed or the time during which a Stock Award or any part thereof will vest in accordance with the Plan, notwithstanding the provisions in the Stock Award stating the time at which it may first be exercised or redeemed or the time during which it will vest.

(b) **Stockholder Rights.** No Participant shall be deemed to be the holder of, or to have any of the rights of a holder with respect to, any shares of Common Stock subject to such Stock Award unless and until such Participant has satisfied all requirements for exercise of the Stock Award pursuant to its terms.

(c) **No Employment or other Service Rights.** Nothing in the Plan or any instrument executed or Stock Award granted pursuant thereto shall confer upon any Participant any right to continue to serve the Company or an Affiliate in the capacity in effect at the time the Stock Award was granted or shall affect the right of the Company or an Affiliate to terminate (i) the

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employment of an Employee with or without notice and with or without cause, (ii) the service of a Consultant pursuant to the terms of such Consultant's agreement with the Company or an Affiliate or (iii) the service of a Director pursuant to the Bylaws of the Company or an Affiliate, and any applicable provisions of the corporate law of the state in which the Company or the Affiliate is incorporated, as the case may be.

(d) **Incentive Stock Option \$100,000 Limitation.** To the extent that the aggregate Fair Market Value (determined at the time of grant) of Common Stock with respect to which Incentive Stock Options are exercisable for the first time by any Optionholder during any calendar year (under all plans of the Company and its Affiliates) exceeds one hundred thousand dollars (\$100,000) (the "*ISO Limit*"), the Options or portions thereof that exceed the ISO Limit (according to the order in which they were granted) shall be treated as Nonstatutory Stock Options, notwithstanding any contrary provision of a Stock Award Agreement; provided however, that to the extent that applicable law is amended to increase or decrease the incentive stock option value limitation, the ISO Limit shall be deemed to be such amended value.

(e) **Investment Assurances.** The Company may require a Participant, as a condition of exercising or acquiring Common Stock under any Stock Award, (i) to give written assurances satisfactory to the Company as to the Participant's knowledge and experience in financial and business matters and/or to employ a purchaser representative reasonably satisfactory to the Company who is knowledgeable and experienced in financial and business matters and that he or she is capable of evaluating, alone or together with the purchaser representative, the merits and risks of exercising the Stock Award; and (ii) to give written assurances satisfactory to the Company stating that the Participant is acquiring Common Stock subject to the Stock Award for the Participant's own account and not with any present intention of selling or otherwise distributing the Common Stock. The foregoing requirements, and any assurances given pursuant to such requirements, shall be inoperative if (1) the issuance of the shares of Common Stock upon the exercise or acquisition of Common Stock under the Stock Award has been registered under a then currently effective registration statement under the Securities Act or (2) as to any particular requirement, a determination is made by counsel for the Company that such requirement need not be met in the circumstances under the then applicable securities laws. The Company may, upon advice of counsel to the Company, place legends on stock certificates issued under the Plan as such counsel deems necessary or appropriate in order to comply with applicable securities laws, including, but not limited to, legends restricting the transfer of the Common Stock.

(f) **Withholding Obligations.** To the extent provided by the terms of a Stock Award Agreement, a Participant may satisfy any federal, state or local tax withholding obligation relating to the exercise or acquisition of Common Stock under a Stock Award or redemption of a SAR or Phantom Stock Award by any of the following means (in addition to the Company's right to withhold from any compensation paid to the Participant by the Company) or by a combination of such means: (i) tendering a cash payment; (ii) authorizing the Company to withhold shares of Common Stock from the shares of Common Stock otherwise issuable to the Participant as a result of the exercise or acquisition of Common Stock under the Stock Award; *provided, however*, that no shares of Common Stock are withheld with a value exceeding the minimum amount of tax required to be withheld by law (or such lower amount as may be

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necessary to avoid variable award accounting); or (iii) delivering to the Company owned and unencumbered shares of Common Stock.

(g) **Information Obligation.** To the extent required by Section 260.140.46 of Title 10 of the California Code of Regulations, the Company shall deliver financial statements to Participants at least annually. This Section 10(g) shall not apply to key Employees whose duties in connection with the Company assure them access to equivalent information.

(h) **Repurchase Limitation.** The terms of any repurchase option shall be specified in the Stock Award, and the repurchase price may be either the Fair Market Value of the shares of Common Stock on the date of termination of Continuous Service or the lower of (i) the Fair Market Value of the shares of Common Stock on the date of repurchase or (ii) their original purchase price. To the extent required by Section 260.140.41 and Section 260.140.42 of Title 10 of the California Code of Regulations at the time a Stock Award is made, any repurchase option contained in a Stock Award granted to a person who is not an Officer, Director or Consultant shall be upon the terms described below:

(i) **Fair Market Value.** If the repurchase option gives the Company the right to repurchase the shares of Common Stock upon termination of Continuous Service at not less than the Fair Market Value of the shares of Common Stock to be purchased on the date of termination of Continuous Service, then (i) the right to repurchase shall be exercised for cash or cancellation of purchase money indebtedness for the shares of Common Stock within ninety (90) days of termination of Continuous Service (or in the case of shares of Common Stock issued upon exercise of Stock Awards after such date of termination, within ninety (90) days after the date of the exercise) or such longer period as may be agreed to by the Company and the Participant (for example, for purposes of satisfying the

requirements of Section 1202(c)(3) of the Code regarding “qualified small business stock”) and (ii) the right terminates when the shares of Common Stock become publicly traded.

(ii) **Original Purchase Price.** If the repurchase option gives the Company the right to repurchase the shares of Common Stock upon termination of Continuous Service at the lower of (i) the Fair Market Value of the shares of Common Stock on the date of repurchase or (ii) their original purchase price, then (x) the right to repurchase at the original purchase price shall lapse at the rate of at least twenty percent (20%) of the shares of Common Stock per year over five (5) years from the date the Stock Award is granted (without respect to the date the Stock Award was exercised or became exercisable) and (y) the right to repurchase shall be exercised for cash or cancellation of purchase money indebtedness for the shares of Common Stock within ninety (90) days of termination of Continuous Service (or in the case of shares of Common Stock issued upon exercise of Options after such date of termination, within ninety (90) days after the date of the exercise) or such longer period as may be agreed to by the Company and the Participant (for example, for purposes of satisfying the requirements of Section 1202(c)(3) of the Code regarding “qualified small business stock”).

## 11. ADJUSTMENTS UPON CHANGES IN STOCK

(a) **Capitalization Adjustments.** If any change is made in, or other event occurs with respect to, the Common Stock subject to the Plan or subject to any Stock Award without the

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receipt of consideration by the Company (through merger, consolidation, reorganization, recapitalization, reincorporation, stock dividend, dividend in property other than cash, stock split, liquidating dividend, combination of shares, exchange of shares, change in corporate structure or other transaction not involving the receipt of consideration by the Company (each a “Capitalization Adjustment”), the Plan will be appropriately adjusted in the class(es) and maximum number of securities subject to the Plan pursuant to Sections 4(a) and 4(b) and the maximum number of securities subject to award to any person pursuant to Section 5(c), and the outstanding Stock Awards will be appropriately adjusted in the class(es) and number of securities and price per share of Common Stock subject to such outstanding Stock Awards. The Board shall make such adjustments, and its determination shall be final, binding and conclusive. (The conversion of any convertible securities of the Company shall not be treated as a transaction “without receipt of consideration” by the Company.)

(b) **Dissolution or Liquidation.** In the event of a dissolution or liquidation of the Company, then all outstanding Options shall terminate immediately prior to the completion of such dissolution or liquidation, and shares of Common Stock subject to the Company’s repurchase option may be repurchased by the Company notwithstanding the fact that the holder of such stock is still in Continuous Service.

(c) **Corporate Transaction.** In the event of a Corporate Transaction, any surviving corporation or acquiring corporation may assume or continue any or all Stock Awards outstanding under the Plan or may substitute similar stock awards for Stock Awards outstanding under the Plan (it being understood that similar stock awards include, but are not limited to, awards to acquire the same consideration paid to the stockholders or the Company, as the case may be, pursuant to the Corporate Transaction), and any reacquisition or repurchase rights held by the Company in respect of Common Stock issued pursuant to Stock Awards may be assigned by the Company to the successor of the Company (or such successor’s parent company), if any, in connection with such Corporate Transaction. In the event that any surviving corporation or acquiring corporation does not assume or continue any or all such outstanding Stock Awards or substitute similar stock awards for such outstanding Stock Awards, then with respect to Stock Awards that have not been assumed, continued or substituted and that are held by Participants whose Continuous Service has not terminated prior to the effective time of the Corporate Transaction, the vesting of such Stock Awards (and, if applicable, the time at which such Stock Awards may be exercised or redeemed) shall (contingent upon the effectiveness of the Corporate Transaction) be accelerated in full to a date prior to the effective time of such Corporate Transaction as the Board shall determine (or, if the Board shall not determine such a date, to the date that is five (5) days prior to the effective time of the Corporate Transaction), the Stock Awards shall terminate if not exercised or redeemed (if applicable) at or prior to such effective time, and any reacquisition or repurchase rights held by the Company with respect to such Stock Awards held by Participants whose Continuous Service has not terminated shall (contingent upon the effectiveness of the Corporate Transaction) lapse. With respect to any other Stock Awards outstanding under the Plan that have not been assumed, continued or substituted, the vesting of such Stock Awards (and, if applicable, the time at which such Stock Award may be exercised or redeemed) shall not be accelerated, unless otherwise provided in a written agreement between the Company or any Affiliate and the holder of such Stock Award, and such Stock Awards shall terminate if not exercised or redeemed (if applicable) prior to the effective time of the Corporate Transaction.

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(d) **Change in Control.** A Stock Award held by any Participant whose Continuous Service has not terminated prior to the effective time of a Change in Control may be subject to additional acceleration of vesting and exercisability or redemption upon or after such event as may be provided in the Stock Award Agreement for such Stock Award or as may be provided in any other written agreement between the Company or any Affiliate and the Participant, but in the absence of such provision, no such acceleration shall occur.

## 12. AMENDMENT OF THE PLAN AND STOCK AWARDS.

(a) **Amendment of Plan.** The Board at any time, and from time to time, may amend the Plan. However, except as provided in Section 11(a) relating to Capitalization Adjustments, no amendment shall be effective unless approved by the stockholders of the Company to the extent stockholder approval is necessary to satisfy the requirements of Section 422 of the Code.

(b) **Stockholder Approval.** The Board, in its sole discretion, may submit any other amendment to the Plan for stockholder approval.

(c) **Contemplated Amendments.** It is expressly contemplated that the Board may amend the Plan in any respect the Board deems necessary or advisable to provide eligible Employees with the maximum benefits provided or to be provided under the provisions of the Code and the regulations promulgated thereunder relating to Incentive Stock Options and/or to bring the Plan and/or Incentive Stock Options granted under it into compliance therewith.

(d) **No Impairment of Rights.** Rights under any Stock Award granted before amendment of the Plan shall not be impaired by any amendment of the Plan unless (i) the Company requests the consent of the Participant and (ii) the Participant consents in writing.

(e) **Amendment of Stock Awards.** The Board at any time, and from time to time, may amend the terms of any one or more Stock Awards; *provided, however,* that the rights under any Stock Award shall not be impaired by any such amendment unless (i) the Company requests the consent of the Participant and (ii) the Participant consents in writing.

## 13. TERMINATION OR SUSPENSION OF THE PLAN.

**(a) Plan Term.** The Board may suspend or terminate the Plan at any time. Unless sooner terminated, the Plan shall terminate on the day before the tenth (10th) anniversary of the date the Plan is adopted by the Board or approved by the stockholders of the Company, whichever is earlier. No Stock Awards may be granted under the Plan while the Plan is suspended or after it is terminated.

**(b) No Impairment of Rights.** Suspension or termination of the Plan shall not impair rights and obligations under any Stock Award granted while the Plan is in effect except with the written consent of the Participant.

**14. EFFECTIVE DATE OF PLAN.**

The Plan shall become effective as determined by the Board, but no Stock Award shall be exercised or redeemed (or, in the case of a stock bonus, shall be granted) unless and until the

Plan has been approved by the stockholders of the Company, which approval shall be within twelve (12) months before or after the date the Plan is adopted by the Board.

**15. CHOICE OF LAW.**

The law of the State of Delaware shall govern all questions concerning the construction, validity and interpretation of this Plan, without regard to such state's conflict of laws rules.

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\* Amended on August 1, 2006 to increase shares reserved to 3,250,000.

Amended on June 25, 2007 to increase shares reserved to 5,387,758.

Amended on February 18, 2009 to increase shares reserved to 5,599,734.

Amended on February 25, 2009 to increase shares reserved to 9,996,108.

Amended on April 16, 2009 to increase shares reserved to [    ].

Amended on August 2, 2011 to increase shares reserved to 10,084,201.

Amended on May 8, 2014 to increase shares reserved to 18,222,157.



**Lonza****Process Development and Manufacturing****Services Agreement****by and between****Proteon Therapeutics****and****Lonza Ltd****Lonza****PROCESS DEVELOPMENT AND MANUFACTURING SERVICES AGREEMENT**

This Process Development and Manufacturing Services Agreement (this "Agreement") is effective as of September 1, 2009 (the "Effective Date"), by and between Proteon Therapeutics, a Delaware corporation, with an address at 200 West Street, Waltham, Massachusetts ("PROTEON"), and Lonza Ltd, a Swiss company with an address at Muenchensteinerstrasse 38, CH-4002 Basel, Switzerland ("LONZA") (each, a "Party" and together the "Parties").

**RECITALS**

WHEREAS, PROTEON intends to develop and commercialize certain products containing a recombinant form of Type 1 human pancreatic elastase as the active pharmaceutical ingredient known by PROTEON as PRT-201 ("API") and wishes to contract with a contract manufacturing organization for the process development, manufacture and supply of API; and

WHEREAS, LONZA has process development, manufacturing and related services experience and expertise and owns a facility that is or would be suitable for production of API; and

WHEREAS, PROTEON desires to retain LONZA as a manufacturer of clinical quantities of API and to purchase process development and manufacturing services to supply clinical quantities of such product from LONZA, and LONZA desires to perform such services for PROTEON, all on the terms and conditions set forth in this Agreement.

**AGREEMENT**

NOW, THEREFORE, in consideration of the mutual promises and covenants herein contained and other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, and intending to be legally bound hereby, the Parties hereto agree as follows:

**ARTICLE 1  
DEFINITIONS**

The following capitalized terms, whether used in the singular or plural, shall have the meanings assigned to them below for purposes of this Agreement:

1.1 "Acquisition Cost" means the actual price paid by LONZA to any Third Party (net of any discounts, rebates, credits or the like) for any materials (including the Raw Materials, Resins, Consumables and Wearables) used in the manufacture of the Drug Substance under this Agreement, including, but not limited to, shipping and handling costs and customs duties incurred and paid by LONZA to that Third Party in connection with the acquisition of such materials, and also including [ ]\* of such actual price to cover LONZA's acquisition and storage costs for such materials.

\* CONFIDENTIAL TREATMENT REQUESTED. OMITTED PORTIONS FILED WITH THE SECURITIES AND EXCHANGE COMMISSION PURSUANT TO RULE 406 PROMULGATED UNDER THE SECURITIES ACT OF 1933, AS AMENDED.

**Lonza**

1.2 "Additional Services" means any service that is not contained in the Project Plan and that requires a Change Order from PROTEON in order to authorize LONZA to commence the same or any service specifically identified as an Additional Service in this Agreement.

1.3 "Affiliate" means, with respect to either Party, any other corporation or business entity that directly, or indirectly through one or more intermediaries, controls, is controlled by or is under common control with such Party. For purposes of this definition, the term "control" means direct or indirect ownership of more than fifty percent (50%) of the securities or other ownership interests representing the equity voting stock or general partnership or membership

interest of such entity or the power to direct or cause the direction of the management or policies of such entity, whether through the ownership of voting securities, by contract, or otherwise.

1.4 “Agreement” has the meaning ascribed to it in the Recitals.

1.5 “API” has the meaning ascribed to it in the Recitals.

1.6 “Batch” means a specific quantity of Drug Substance produced from a single Run.

1.7 “Batch Disposition Documentation” means all of the documentation associated with the production and testing of a given clinical Batch, including without limitation production records, sampling documentation, test results, Investigative and Corrective Action Reports, deviation reports, all applicable Manufacturing Process data (including any pertinent output from instrumentation), the Certificate of Analysis, the Certificate of Compliance and any additional Quality Review and Approval documentation, if applicable.

1.8 “Business Days” means any day other than a Saturday or Sunday that is not a national holiday in the United States or Switzerland.

1.9 [ ]\*

1.10 “Certificate of Analysis” means a document prepared by LONZA listing tests performed by LONZA or approved Subcontractors, the specifications and test results.

1.11 “Certificate of Compliance” means a document prepared by LONZA: (i) listing the manufacturing date, unique Batch number, and quantity of Drug Substance in such Batch, (ii) certifying that such Batch was manufactured in accordance with the Master Production Record and cGMP and (iii) certifying that all Investigative and Corrective Action Reports are completed and approved. The Parties shall from time to time agree upon a format or formats for the Certificate of Compliance to be used under this Agreement.

1.12 “cGMP” means the regulatory requirements for current good manufacturing practices promulgated by the FDA under 21 C.F.R. §§ 210, 211 (as applicable to bulk drug substance only) and ICH, Guidance for Industry Q7A Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients, as the same may be amended from time to time, as well as any additional regulatory agency requirements needed to seek registration in the EU, such as Part II of Volume IV of the EU Guide to Good Manufacturing Practice.

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1.13 “Change Order” means a document mutually approved in writing by both Parties in accordance with the procedures set forth in Section 3.4 that describes in reasonable detail an amendment or modification to the Project and/or the Project Plan.

1.14 “PROTEON Change Request” has the meaning ascribed to it in Section 3.4.

1.15 “LONZA Change Request” has the meaning ascribed to it in Section 3.4.

1.16 “PROTEON Confidential Information” means any Manufacturing Documentation provided by PROTEON to LONZA, and all elements of the Manufacturing Process provided by PROTEON to LONZA, clinical data and information, business plans, regulatory and Product information, Product strategies and all technical and other information, whether patented or unpatented, relating to PROTEON Product processes, test methods, operations, technologies, forecasts and business information that is disclosed or supplied to LONZA by or on behalf of PROTEON pursuant to this Agreement. PROTEON Confidential Information shall also include the Master Production Record, the Materials Specifications, and the Manufacturing Documentation.

1.17 “PROTEON Equipment” means those certain pieces of equipment described in the Project Plan used to produce the Product that are purchased by PROTEON or for which PROTEON reimburses LONZA, including, without limitation, the related documentation regarding the design, validation, operation, calibration and maintenance of such equipment.

1.18 “PROTEON Intellectual Property” means all Intellectual Property owned or Controlled by PROTEON that are conceived, discovered, developed, generated, created, made or reduced to practice or fixed in a tangible medium of expression at any time prior to the Effective Date or after the Effective Date if such Intellectual Property rights are not based upon or related to the performance of the Project.

1.19 “Clinical Batch” means a Batch produced from a Clinical Run.

1.20 “Clinical Run” means a Run manufactured in accordance with the Master Production Record and is used to create Drug Substance for clinical use.

1.21 “Commercially Reasonable Efforts” means with respect to any objective of a Party, diligent, good faith efforts to accomplish such objective, to be undertaken in accordance with such Party’s reasonable business, legal and scientific judgment, consistent with the effort a reasonably comparable biological development company (in the case of PROTEON) or biopharmaceutical contract manufacturer (in the case of LONZA) would normally use to accomplish a similar objective under similar circumstances.

1.22 “Confidentiality Agreement” means the Reciprocal Confidentiality Agreement between PROTEON and Lonza Biologics, Inc., dated May 20th, 2009.

1.23 “Confidential Information” means PROTEON Confidential Information and/or LONZA Confidential Information, as the context requires, except any portion thereof which: (a) is known to the receiving party, as evidenced by the receiving party’s prior written records,

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before receipt thereof under this Agreement; (b) is disclosed to the receiving party by a third person who is under no obligation of confidentiality to the disclosing party with respect to such information and who otherwise has a right to make such disclosure; (c) is or becomes generally known in the public domain through no fault of the receiving party; or (d) is independently developed by the receiving party, as evidenced by the receiving party’s written records, without access to the other Party’s Confidential Information.

1.24 “Conforming Drug Substance” means Drug Substance that conforms to all of the warranties set forth in Section 14.2.1.

1.25 “Consumable” means all bags, liners and other single use or regularly replaced materials that are required to perform the Manufacturing Process (excluding Raw Materials, Resins and Wearables).

1.26 “Control” or “Controlled” means, with respect to any Intellectual Property, the possession (whether by ownership, license, or other agreement or arrangement existing now or after the Effective Date, other than pursuant to this Agreement) by a Party or an Affiliate thereof of the right to grant to the other Party a license as provided herein under such Intellectual Property without violating (a) any law or governmental regulation applicable to such license or sublicense or (b) the terms of any agreement or other arrangement with any Third Party that exists as of the Effective Date or, if such right is acquired after the Effective Date, as of the date the Party or an Affiliate thereof first gained possession of such right.

1.27 “Decision Request” has the meaning ascribed to it in Section 3.1.2.

1.28 “Designated Carrier” means the common carrier selected by PROTEON to take delivery of Drug Substance at the LONZA Facility.

1.29 “Drug Substance” means API in bulk form that has been manufactured by LONZA pursuant to this Agreement.

1.30 “Effective Date” has the meaning ascribed to it in the Recitals.

1.31 “EMEA” means the European Medicines Agency, or any successor agency thereto.

1.32 “Engineering Batch” means a Batch produced from an Engineering Run.

1.33 “Engineering Run” means a Run used for process demonstration and engineering of some or all of the Manufacturing Process steps.

1.34 “EXW” means “Ex Works (named place)”, as that expression is defined in *Incoterms 2000*, ICC Publishing S.A.

1.35 “FDA” means the United States Food and Drug Administration, or any successor agency thereto.

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1.36 “FDCA” has the meaning ascribed to it in Section 14.2.1.

1.37 “Force Majeure Event” has the meaning ascribed to it in Section 19.1.

1.38 “Governmental Authority” means any national, multi-national, regional, state or local regulatory agency, department, bureau, or other governmental entity.

1.39 “Indemnitee” has the meaning ascribed to it in Section 15.3.1.

1.40 “Indemnitor” has the meaning ascribed to it in Section 15.3.1.

1.41 “Intellectual Property” means all worldwide (i) Patents, (ii) copyright registrations and applications and all renewals and extensions thereof, (iii) discoveries, inventions, trade secrets, know-how, techniques, methodologies, modifications, improvements, works of authorship, designs and data (whether or not protectable under patent, copyright, trade secrecy or similar laws), and (iv) Confidential Information, including all applications and registrations with respect to the items identified in clauses (iii)-(iv) (if any), but excluding all trademarks, trade names, service marks, logos and other corporate identifiers.

1.42 “Investigative and Corrective Action Reports” or “ICAR” means the document that is used to record the investigation of, as well as the review and disposition of, a failure related to a cGMP manufacturing process or system.

1.43 “Liabilities” has the meaning ascribed to it in Section 15.1.

1.44 “LONZA” has the meaning ascribed to it in the Recitals.

1.45 “LONZA Confidential Information” means all technical and other information, whether patented or unpatented, relating to the LONZA Facility and/or LONZA processes, methods, operations, technologies, forecasts and business information that is disclosed or supplied to, or used on behalf of, PROTEON by LONZA pursuant to this Agreement, or of which PROTEON may become aware through the presence of its employees or agents at LONZA offices or at the LONZA Facility, including, without limitation, trade secrets, know-how, processes, concepts, experimental methods and results and business and scientific plans and information and facility layout and schematics.

1.46 “LONZA Facility” means the facility owned and operated by LONZA at Rottenstrasse 6, 3930 Visp, Switzerland or such other facility designated by LONZA and owned and operated by an Affiliate of LONZA.

1.47 “LONZA Intellectual Property” means all Intellectual Property owned or Controlled by LONZA that are conceived, discovered, developed, generated, created, made or reduced to practice or fixed in a tangible medium of expression at any time prior to the Effective Date or after the Effective Date if such Intellectual Property rights are not based upon or related to the performance of the Project.

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1.48 “Manufacturing Documentation” means all documents and records describing or otherwise related to the Manufacturing Process, other than those embodied in the Master Production Record.

1.49 “Manufacturing Process” means the production process for the manufacture of Drug Substance, as such process may be changed from time to time in accordance with this Agreement.

1.50 [ ]\*

1.51 “Master Production Record” or “MPR” means the document, proposed by LONZA and approved by PROTEON, that defines the manufacturing methods, test methods, specifications, materials, and other procedures, directions and controls associated with the manufacture and testing of Drug Substance. The Master Production Record shall also include or incorporate by reference, without limitation, such information as Materials Specifications, in process and final Drug Substance sampling standards, equipment and instrumentation specifications and standard operating procedures, including, without limitation, standard operating procedures for in-process quality control testing.

1.52 “Materials Specification” or “MS” means a document detailing the specifications for each Raw Material, Resin or Consumable, each as mutually approved by the Parties.

1.53 “NDA” means a new drug application for the Product, or any equivalent filing thereto, filed with the FDA, and any supplements or amendments to any of the foregoing.

1.54 “Non-Conforming Drug Substance” means Drug Substance that fails to conform to all of the warranties set forth in Section 14.2.1.

1.55 “PAI” has the meaning ascribed to it in Section 4.6.

1.56 “Patents” shall mean, with respect to an invention, any patent or patent application, and any patent issuing there from, together with any extensions, reissues, reexaminations, substitutions, renewals, divisions, continuations and continuations-in-part thereof, and any patent or patent application claiming priority to any application in common with any such patent containing a disclosure substantially similar to that of any such patent, all to the extent the foregoing contain claims covering such invention.

1.57 “Product” means the final dosage form of the Drug Substance.

1.58 “Project” means the full range of development and manufacturing services to be provided under this Agreement as more fully described in the Project Plan.

1.59 “Project Administration” has the meaning ascribed to it in Section 3.3.1.

1.60 “Project Intellectual Property” means, individually and collectively, all Intellectual Property conceived, created, discovered, developed, generated, made or reduced to practice or

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fixed in a tangible medium of expression as part of or based upon or related to activities undertaken as part of the Project whether: (a) solely by one or more employees or agents or Subcontractors of LONZA; (b) solely by one or more employees or agents of PROTEON; or (c) jointly by one or more employees or agents or Subcontractors of LONZA and one or more employees or agents of PROTEON.

1.61 “Project Manager” has the meaning ascribed to it in Section 3.2.2.

1.62 “Project Plan” means the scope of work for technology transfer, process development, process implementation, manufacturing and overall project scope, attached as Exhibit A hereto and hereby incorporated into this Agreement by reference.

1.63 “Project Rates” means the applicable rates at which LONZA will charge PROTEON for the various Additional Services performed hereunder, if any, which shall be comparable to the rates utilized by LONZA to price the Project as of the Effective Date.

1.64 “PROTEON” has the meaning ascribed to it in the Recitals.

1.65 “PROTEON Credit” has the meaning ascribed to it in Section 6.1.

1.66 “Quality Agreement” means the quality agreement between the Parties. The Quality Agreement will be negotiated and entered into by the Parties within thirty (30) days following the Effective Date and will be attached as Exhibit C hereto and incorporated into this Agreement by reference.

1.67 “Quality Review and Approval” means LONZA’s review and approval, by LONZA’s quality assurance department, of a Clinical Batch and the associated Batch Disposition Documentation.

1.68 “Raw Material” means all ingredients, solvents and other components of the Drug Substance required to perform the Manufacturing Process (excluding any Consumables, Resins and Wearables).

1.69 “Recall” has the meaning ascribed to it in Section 11.1.

1.70 “Reference Materials” means Drug Substance that is generated from a Run that is well characterized, packaged and stored in a controlled manner, and used as a standard or reference for analytical testing purposes.

1.71 “Registration” has the meaning ascribed to it in Section 8.1.

1.72 “Regulatory Authority” means the FDA or the EMEA, or both of the foregoing, as the case requires.

1.73 “Regulatory Filing” means any or all applications, including but not limited to the NDA, submitted to Regulatory Authorities for the purpose of registering the Product or the Manufacturing Process as required by statute, and any amendments or supplements thereto,

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and any other filings required by the Regulatory Authorities relating to the manufacture, testing, sale or distribution of the Product.

1.74 “Replacement Drug Substance” has the meaning ascribed to it in Section 10.3.

1.75 “Resin” means all chromatographic media intended to refine or purify the Drug Substance, as specified in the Master Production Record.

1.76 “Rules” has the meaning ascribed to it in Section 20.3.

1.77 “Run” means a single complete operation of all, or a discreet portion of, the Manufacturing Process at the LONZA Facility.

1.78 “Shipping Guidelines” means LONZA’s written procedures, as approved by PROTEON in writing, that describe the methods of packaging, preserving, monitoring and shipping any and all PROTEON property, including the Drug Substance.

1.79 [ ]\*

1.80 “Subcontractor” means any independent entity that LONZA contracts with to perform any services or meet any obligations that are required under the terms and conditions of this Agreement.

1.81 “Suite Activation Date” has the meaning ascribed to it in Section 18.2.

1.82 “Term” has the meaning ascribed to it in Section 18.1.

1.83 “Third Party” means any party other than PROTEON, LONZA and their respective Affiliates.

1.84 “Transfer Batch” means a Batch produced from a Transfer Run.

1.85 “Transfer Run” means a Run used to demonstrate and transfer in to LONZA the Manufacturing Process.

1.86 “Waste” shall mean any “hazardous substance” and/or “hazardous material” as provided under the Comprehensive Environmental Response, Compensation and Liability Act (CERCLA), any “hazardous waste” as provided under the Resource Conservation and Recovery Act (RCRA), and/or any other waste material, pollutant and/or contaminant of any kind including, without limitation, any routine process waste or any by-product arising from any activities conducted pursuant to this Agreement.

1.87 “Wearables” means any coverings or protective gear used by LONZA employees or agents in the course of the performing the development and manufacturing services hereunder, including without limitation gloves, coveralls, booties, eye shields and the like.

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1.88 [ ]\*

## ARTICLE 2 COMMITMENT TO DEVELOP AND MANUFACTURE; PURCHASE

### 2.1 Commitment to Develop and Manufacture.

2.1.1 Development. PROTEON hereby retains LONZA to develop the Manufacturing Process at the LONZA Facility, LONZA shall use Commercially Reasonable Efforts to develop the same, and PROTEON shall pay LONZA for such development work, all in accordance with the Project Plan and Exhibit B.

2.1.2 Manufacture. Subject to the successful completion of the development of the Manufacturing Process at the LONZA Facility as defined in the Project Plan, PROTEON retains LONZA as a manufacturer of Drug Substance. LONZA shall provide sufficient services and capacity to manufacture Drug Substance for PROTEON in accordance with the Project Plan and in accordance with the Master Production Record, and PROTEON shall purchase such services and capacity from LONZA in accordance with the Project Plan and Milestone Payment Summary (Exhibits A&B).

## ARTICLE 3 PROJECT PLAN; PROJECT MANAGEMENT

3.1 Project Plan. In order to enable the Parties to fulfill their respective obligations under this Agreement, the Parties shall implement and perform their obligations as set out in the Project Plan. The Project Plan will be written by LONZA and submitted for PROTEON approval.

3.1.1 The Project Plan may be amended by agreement of the Parties through the Change Order procedures set forth in Section 3.4. In the case of a Change Order to a Project Plan, that Change Order becomes the controlling document.

3.1.2 LONZA may from time to time notify PROTEON that LONZA requires approvals or other actions by PROTEON relating to the services that do not represent a change in the terms of the Project Plan (each, a “Decision Request”). Adherence to the time-scales set out in the Project Plan is contingent in part on PROTEON’s reasonably expedient review and response to such Decision Requests. When making a Decision Request, LONZA shall provide PROTEON with written notice that includes a description of the approval that it is seeking and copies of the requisite documents, data and development paths to which such approval relates. PROTEON shall respond to each Decision Request notice within the period of time specified in the Decision Request notice (not to be less than one (1) Business Day nor more than two (2) Business Days after PROTEON has received from LONZA the Decision Request and the requisite documents, data and development paths). Any change from an approved Decision Request shall be subject to the procedures specified in Section 3.4. If PROTEON’s decision on a Decision Request affects the

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services specified in the Project Plan, then PROTEON shall issue a PROTEON Change Request and such PROTEON Change Request shall be subject to the procedures specified in Section 3.4.

### 3.2 Project Management

3.2.1 **This Section Intentionally Omitted.**

3.2.2 The daily interactions and management with respect to the Project will be performed by two project managers, one appointed by each Party and each one having the authority to manage the Project in conjunction with the other Project Manager and to further the daily tasks and goals of each Party (each, a "Project Manager").

3.2.3 The Project Managers shall be the principle points of contact between the Parties. As part of their duties, the Project Managers shall be responsible for monitoring and revising the Project Plan (in accordance with the procedures set forth in Section 3.4, responding to Decision Requests (in the case of PROTEON), establishing operating guidelines for the Project, defining communication formats, forming and approving Project teams and monitoring the general progress of the Project.

3.2.4 The Project Managers shall be appointed by each respective Party no later than August 17, 2009. The LONZA Operations executive responsible for the early phase tasks may continue in the role of Project Manager for a designated period of time, as agreed to by PROTEON.

3.2.5 Neither Party shall remove or replace its Project Manager without giving 30 days notice in writing to the other Party; provided that, such removal or replacement may be made with less than thirty (30) days notice where such person has left the employment of the relevant Party, where such Person has taken a leave of absence, where such Person is out on disability or sick leave for more than a two-week period, or if the other Party agrees in writing to such removal or replacement.

### 3.3 Project Administration

3.3.1 "Project Administration" tasks include, but are not limited to, meeting attendance, document review, document approval and project consultation.

3.3.2 All hours invoiced for Project Administration must be attributed to tasks directly related to the Project and incurred only by LONZA employees who have been pre-approved by the PROTEON to accrue Project Administration hours. LONZA will submit a list of employees to PROTEON for approval. The pricing quoted in Exhibit A includes Project Administration costs and such Project Administration services shall not constitute Additional Services.

3.4 Project Change Order Process. (a) Any amendments or modifications to the services specified in the Project Plan shall be set forth in writing in a Change Order mutually agreed upon by the Parties using the procedure set forth in this Section 3.4. During the Project, PROTEON may request amendments to the Project Plan to effect changes in the services specified in the Project Plan. If PROTEON wishes to make a change it shall notify LONZA of the requested change specifying the change with sufficient details to enable

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LONZA to evaluate it (a "PROTEON Change Request"). Within five (5) Business Days following the date of LONZA's receipt of a PROTEON Change Request, LONZA shall deliver a Change Order document that: (i) assesses the impact of the change on the schedule, and (ii) incorporates a description of the requested change and the cost therefor.

(b) Within five (5) Business Days following PROTEON's receipt of a LONZA Change Order ("Response Period"), PROTEON will notify LONZA whether or not it accepts the Change Order. If PROTEON accepts the Change Order, then the provisions of this Agreement shall be deemed amended to incorporate such change in accordance with the Change Order. If PROTEON notifies LONZA not to proceed within the Response Period, then the PROTEON Change Request shall be deemed withdrawn and LONZA shall take no further action in respect of it. If LONZA has not received any notice by the expiration of the Response Period, then PROTEON shall be deemed to have advised LONZA not to proceed, A separate Change Order will be required for each PROTEON Change Request but a PROTEON Change Request may include multiple changes; and each Change Order will become subject to this Agreement when signed by LONZA and PROTEON. Change Orders shall be implemented as soon as commercially practicable to do so. PROTEON shall be responsible for payment of any price increase resulting from any such Change Order, which shall be priced on a time and materials basis, as mutually agreed upon by the Parties; provided such pricing shall be based upon the Project Rates.

(c) LONZA may not make any changes in the Project Plan without PROTEON's prior written approval, which shall not be unreasonably withheld. LONZA may recommend amendments to the Project Plan to effect changes in the services specified in the Project Plan if necessary to respond to difficulties encountered in achieving the technical objectives of the Project. If LONZA wishes to recommend a Change Request, it shall notify PROTEON of the requested change in accordance with LONZA's SOP and provide PROTEON with a LONZA Change Request and a Change Order and the provisions of Section 3.4(a)-(b) shall apply.

## ARTICLE 4 SERVICES

4.1 Quality Agreement. The Quality Agreement specifies certain testing, storage, release, cGMP, regulatory and other quality assurance requirements relating to manufacture and shipment of Drug Substance by LONZA under this Agreement, all of which shall be deemed a material part of this Agreement.

4.2 LONZA Facility. All Drug Substance manufactured for PROTEON hereunder shall be manufactured by LONZA at a LONZA Facility. LONZA shall be solely responsible for all scheduling related to the LONZA Facility and for the operation of such facility.

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4.4 Transfer and Engineering Runs. If called for in the Project Plan, LONZA shall perform manufacture Transfer Batches and/or Engineering Batches in accordance with the Project Plan.

4.5 Raw Materials and Consumables.

4.5.1 Procurement. Unless specifically stated otherwise in the Project Plan, LONZA shall be responsible for the procurement of all Raw Materials, Resins, Consumables and Wearables necessary for the manufacture of the Drug Substance. LONZA shall not be responsible for delays in the purchase and/or delivery of Raw Materials, Resins, and Consumables that occur despite LONZA using Commercially Reasonable Efforts to avoid such delays. All Raw Materials, Resins, Consumables and Wearables shall be invoiced to PROTEON by LONZA at the relevant Acquisition Cost.

4.5.2 Compliance with Specifications. All Raw Materials, Resins and Consumables used in the Manufacturing Process shall comply with the applicable Materials Specifications, or as otherwise agreed in writing by the Parties. LONZA or a Subcontractor approved in accordance with Section 4.8 shall perform testing and evaluation of the Raw Materials, Resins and Consumables as required to meet the foregoing obligations.

4.5.3 PROTEON Equipment. At PROTEON's request, LONZA shall use PROTEON's Equipment and PROTEON shall reimburse LONZA for the acquisition, installation and validation of PROTEON Equipment in accordance with the Project Rates. However, PROTEON shall not be required to reimburse LONZA for the costs of acquiring PROTEON Equipment under this Agreement if PROTEON paid for such PROTEON Equipment directly or if PROTEON has already reimbursed LONZA for such costs.

4.6 Retention and Reserve Samples. LONZA shall identify and retain certain reserve samples of all Raw Materials and intermediate production samples generated in the production of Clinical Batches as set forth in the applicable Materials Specifications, the applicable standard operating procedures, the Master Production Record or as otherwise agreed in writing by LONZA and PROTEON.

4.7 Handling of Materials; Wastes. PROTEON must notify LONZA of any hazardous conditions or Wastes known to PROTEON that may exist or be produced by LONZA in the course of performing the services contemplated by this Agreement. At PROTEON's expense, LONZA or a designated Third Party contractor shall handle, label, package, store, transport and dispose of all Wastes generated through performance of the manufacturing and processing activities hereunder in material compliance with all Federal, state and local laws, rules, and regulations applicable to such handling, labeling, packaging, storage, transport and disposal. Each Party shall promptly notify the other of any health hazards or potential health hazards of

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which it is or becomes aware concerning exposure to or handling of the Raw Materials, Drug Substance or Wastes.

4.8 Approval of Subcontracting. LONZA shall not subcontract or otherwise delegate all or any portion of its obligations under this Agreement without PROTEON's prior written approval. Notwithstanding the foregoing, LONZA may subcontract certain non-essential or routine tasks without PROTEON's consent (e.g., janitorial services, electrical upgrades, etc.). Any work relevant to the Project Plan subcontracted or delegated to a Third Party in accordance with this Section shall be invoiced to PROTEON by LONZA at cost.

4.9 Document Changes. Any requests by LONZA or PROTEON for changes to documents which are part of LONZA's cGMP documentation system, including but not limited to the Master Production Record and any standard operating procedures or Materials Specifications, will be handled by a Change Request using the procedures in Section 3.4.

**ARTICLE 5  
DELIVERIES**

5.1 Delivery Terms. LONZA will deliver each Clinical Batch EXW LONZA's Visp Facility to the Designated Carrier in accordance with the Shipping Guidelines; provided that risk of loss in and title to the Clinical Batch shall pass to PROTEON when the Clinical Batch is placed upon the Designated Carrier's vehicle. PROTEON shall arrange for shipment and take delivery of such Batch from LONZA's Facility via the Designated Carrier, at PROTEON's expense, within five (5) Business Days after PROTEON's acceptance of a Clinical Batch pursuant to Article 10, or pay applicable storage costs. LONZA shall provide storage for such Batch in accordance with the [ ]\* at no charge during such five (5) business day period; provided, that any additional storage beyond such five (5) business day period will be charged to PROTEON as Additional Services in accordance with the Project Rates. Notwithstanding anything to the contrary contained in this Agreement, in no event shall LONZA be required to store any Clinical Batch for more than twenty (20) calendar days after PROTEON's acceptance of such Batch pursuant to Article 10. LONZA shall not be required to deliver any Batch to the Designated Carrier until the Designated Carrier informs LONZA that it has obtained all appropriate approvals and consents of any Gown-mental Authority necessary for the transportation or shipment of such Batch,

**ARTICLE 6  
PAYMENTS**



6.1 Compensation. For each deliverable specified in the Project Plan, PROTEON shall pay to LONZA the milestone payment amount corresponding to such deliverable, as set forth in the Project Plan. Each milestone payment shall become due and payable upon the completion by LONZA of the applicable deliverable. No milestone payment shall be contingent upon completion of any subsequent deliverable. In addition, PROTEON shall pay for any Acquisition Costs and Additional Services in accordance with the Project Rates, unless otherwise agreed to by the Parties.

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6.2 Payment Terms. All invoices for completed stages and/or substages shall be issued within thirty (30) days after the applicable completion date. All amounts due thereunder shall be due and payable within thirty (30) days after receipt of such invoice. In the event that PROTEON has not paid an invoice within thirty (30) Business Days of the applicable due date (as established by the preceding sentences), PROTEON's failure shall be considered a material breach under Section 18.3.1, subject to the cure provisions set forth therein. Payments shall be made by wire transfer or check in U.S. currency. Past due amounts shall bear interest from the date due until paid at a rate equal to the lesser of twelve percent (12%) per annum, or the maximum rate permitted by applicable law. PROTEON shall not be considered to be in breach of Section 18.3.1 with respect to payments that PROTEON contests in good faith using the procedures in Section 20.3 during the pendency of such dispute; provided that in the event PROTEON does not prevail in such dispute then interest shall accrue from the date payment was due until the date PROTEON makes payment and such payment shall when made shall be accompanied by all interest so accrued.

6.3 Currency and Exchange Rate. All invoices submitted to PROTEON pursuant to Section 6.2 shall be paid by PROTEON in U.S. Dollars (USD) based on the conversion of each payment amount scheduled in the Swiss Francs (CHF) denominated Milestone Payment Schedule in Exhibit B to USD, utilizing the base exchange rate, as described in the next sentence, or as otherwise adjusted pursuant to this Section 6.3. The base exchange rate for this Agreement will be that for purchasing CHF with USD at closing on the Effective Date of the Agreement as stated in the *Wall Street Journal*, Eastern Edition. If the exchange rate, as stated in the *Wall Street Journal*, Eastern Edition, for purchasing CHF with USD increases or decreases by 5% or less from the base exchange rate at any date of invoice then no adjustment shall be made; if the exchange rate for purchasing CHF with USD increases or decreases by more than 5% from the base exchange rate at any date of invoice, then LONZA shall continue to bear the burden or benefit of the first 5% increase or decrease, and the Parties shall each assume 50% of the burden or the benefit of such increase or decrease greater than 5%.

6.4 Taxes. The pricing under this Agreement includes all duties and taxes, however designated, levied or based on this Agreement or the services delivered hereunder, including, without limitation, any personal property, sales, goods and services, use or value added taxes whether such taxes are now in force or subsequently levied. PROTEON shall not be responsible for any taxes (excluding taxes based on PROTEON's net income and FICA, workers' compensation, unemployment and withholding taxes concerning PROTEON personnel) with respect to the transactions contemplated by this Agreement. The Parties will cooperate to minimize, to the extent legally permissible, the tax liabilities related to this Agreement. Notwithstanding the foregoing, such cooperation shall not cause any adverse tax consequences to be incurred by either Party which would not have otherwise been incurred under the provisions of this Agreement, including this Section 6.3.

## ARTICLE 7 MANUFACTURING AUDITS

During regular business hours and upon at least four (4) weeks prior notice to LONZA, PROTEON shall have the right to perform, directly or through its representatives (agreed with

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LONZA in advance), certain manufacturing audits as set forth in the Quality Agreement, or as otherwise agreed in writing by LONZA and PROTEON. All LONZA personnel time and resources necessary to complete the first manufacturing audit for a calendar year shall be provided at no cost to PROTEON; provided, however, any LONZA personnel time and resources necessary to complete any additional manufacturing audits (over and above one) in that same year shall be invoiced to PROTEON as Additional Services in accordance with the Project Rates, unless such additional audits are reasonably deemed necessary by PROTEON as a result of findings of the first audit. PROTEON shall be responsible for all Third Party costs of all manufacturing audits. Audits shall not exceed three (3) Business Days with no more than 2 sub-groups of Auditors.

## ARTICLE 8 REGULATORY MATTERS

8.1 Permits. LONZA shall secure and maintain in good order, at its sole cost and expense, such current governmental registrations, permits and licenses as are required by Governmental Authorities in order for LONZA to perform all of its obligations under this Agreement (including, without limitation, Annual Registration of Drug Establishment registrations (Form FDA 2656e) granted by the FDA and any comparable registrations granted by any other Regulatory Authority) (each, a "Registration"), for so long and insofar as is necessary to permit LONZA to perform any of its obligations under this Agreement. Notwithstanding the foregoing, PROTEON shall be responsible for reimbursing LONZA for the cost of any permits that are solely and specifically required to manufacture the Drug Substance.

8.2 Regulatory Documentation. Any PROTEON requests for documents or other work product that do not exist as of the date of such request or other substantive requests for assistance in compiling any Regulatory Filing shall constitute Additional Services, and LONZA shall notify PROTEON of the same, and, if PROTEON authorizes such services, LONZA shall prepare a Change Order and invoice PROTEON for such Additional Services in accordance with the Project Rates.

8.3 Regulatory Communications and Correspondence. Any and all communications from and to the FDA or other Regulatory Authorities related to the Product or to the manufacture of the Drug Substance at the LONZA Facility shall be handled in accordance with the terms and conditions of the Quality Agreement, or as otherwise agreed in writing by LONZA and PROTEON.

8.4 Ownership of Regulatory Filings. PROTEON shall be the sole owner of all Regulatory Filings and all governmental approvals obtained by PROTEON from any Regulatory Authority with respect to the Drug Substance or the Product.

8.5 Health and Safety Information. PROTEON shall provide LONZA with all information in PROTEON's possession or control concerning any health hazards or potential health hazards associated with exposure to or the handling, storage, use or disposal of Drug Substance, including, without limitation, a Material Safety Data Sheet for Drug Substance. In

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the event that any such information is updated or corrected, PROTEON shall promptly notify LONZA thereof and provide LONZA with the updated or corrected information.

8.6 Regulatory Authorities. PROTEON shall be responsible for handling all complaints and communications from Regulatory Authorities with respect to the Drug Substance and/or Product. As reasonably requested by PROTEON, LONZA shall cooperate in resolving such complaints and responding to such communications to the extent they pertain to the Drug Substance and/or Product. PROTEON shall reimburse LONZA for all reasonable costs and expenses incurred by LONZA in connection with the performance of LONZA's obligations under this Section.

#### ARTICLE 9 QUALITY ASSURANCE; QUALITY CONTROL

Responsibility for Quality Assurance and Quality Control. Responsibility for quality assurance and quality control of Drug Substance shall be allocated between PROTEON and LONZA as set forth in the Quality Agreement.

#### ARTICLE 10 NON-CONFORMANCE

10.1 Notice of Nonconformity. LONZA shall provide PROTEON's quality assurance department with copies of completed Batch Disposition Documentation, and shall endeavor to do so within ten (10) Business Days of Quality Review and Approval. Within thirty (30) days after PROTEON's receipt of such Batch Disposition Documentation, PROTEON shall determine by review of such Batch Disposition Documentation whether or not the given Clinical Batch conforms to the warranties set forth in Section 14.2.1; provided that LONZA provides timely answers to information requests and resolution of issues arising from PROTEON's review of such Batch Disposition Documentation (and the thirty (30) day period shall be extended to account for LONZA's failure to provide timely answers to information requests and resolution of such issues). If within the thirty (30) day period, PROTEON's quality assurance department makes a determination that PROTEON believes such Batch to be nonconforming, PROTEON shall have the right to reject such Batch in its entirety and shall notify LONZA in writing within such thirty (30) day period. Such written notice shall specify the manner in which the Clinical Batch fails to conform to the warranties set forth in Section 14.2.1. If PROTEON does not submit written notice of rejection within such thirty (30) day period, such Batch will be deemed to be a Conforming Drug Substance and accepted by PROTEON; provided that such failure to notify shall not prejudice PROTEON's right to reject or revoke acceptance of the Batch if the non-conforming condition which justifies rejection could not have been detected by PROTEON's inspection undertaken pursuant to this Section 10.1; and provided further that the warranty provided in Section 14.2 and LONZA's obligations under Section 15.2 shall survive acceptance of the Batch by PROTEON. In the event that PROTEON desires to accept such Batch prior to the end of the thirty (30) day period, PROTEON will fax written notice of such acceptance to LONZA's Project Manager.

10.2 No LONZA Liability. If PROTEON issues a notice of rejection of a Clinical Batch pursuant to Section 10.1 or revokes its acceptance of a Clinical Batch pursuant to

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Section 10.1, the Parties shall conduct an investigation of such non-conformance in accordance with each Party's standard operating procedures relating to same. In the event that, after such investigation and retesting, if any, LONZA does not confirm such non-conformity, the parties shall agree to conduct an audit of the investigation relating to such Clinical Batch or otherwise in a good faith attempt to agree upon a settlement of the issue. In the event that the parties cannot resolve the issue, a qualified and independent arbitrator selected jointly by LONZA and PROTEON shall review the matter and provide a written decision that shall, save for

manifest error on the face of the decision, be binding on both LONZA and PROTEON. If it is determined pursuant to this Section 10.2 that the Clinical Batch is Conforming Drug Substance, then LONZA shall have no liability to PROTEON with respect to such Clinical Batch, and PROTEON shall pay for such Clinical Batch and for the fees associated with any dispute regarding the Clinical Batch shall be treated in all other respects under this Agreement as though it conformed with all of the warranties set forth in Section 14.2.1 of this Agreement.

10.3 LONZA Liability for Non-Conforming Drug Substance; Replacement. If PROTEON issues a notice of rejection of a Clinical Batch pursuant to Section 10.1 or revokes its acceptance of a Clinical Batch pursuant to Section 10.1 and the Parties or a qualified and independent arbitrator selected using the procedure specified in Section 10.2 determine that such Batch is Non-Conforming Drug Substance, then LONZA shall, as soon as it is commercially practicable to do so, replace such Non-Conforming Drug Substance with Conforming Drug Substance (the "Replacement Drug Substance"). Delivery of Replacement Drug Substance shall be at no additional charge to PROTEON. Notwithstanding anything to the contrary contained herein, delivery of Replacement Drug Substance shall be PROTEON's sole remedy with respect to the Drug Substance, and in furtherance thereof PROTEON waives all other remedies at law or in equity. LONZA shall pay for the fees associated with any dispute regarding a Clinical Batch that is determined to be Nonconforming Drug Substance.

10.4 Cooperation in Investigations; Disposition of Non-Conforming Drug Substance. Each Party shall act in good faith and shall cooperate with the other Party, with any qualified independent Third-Party laboratory in connection with an investigation, and with the arbitrator, as to the existence of or source of nonconformity with respect to a Clinical Batch supplied under this Agreement. In testing the Batch, any independent Third-Party laboratory shall use analytical testing methods as agreed upon by the Parties. At PROTEON'S election, LONZA shall either (i) dispose of any Non-Conforming Drug Substance in accordance with all relevant laws, rules and regulations with respect to such disposal, at LONZA's cost if LONZA was liable for the nonconformity in accordance with Section 10.3 and at PROTEON's cost if LONZA was not liable for the nonconformity in accordance with Section 10.2, or (ii) deliver the Non-Conforming Drug Substance to PROTEON in accordance with Section 5.1.

10.5 Replacement Clinical Batches. In addition to its obligations under Section 10.3 with respect to production and delivery of Replacement Drug Substance, LONZA will, upon PROTEON's request and at PROTEON's expense, use Commercially Reasonable Efforts to produce additional Clinical Batches in cases where a Clinical Batch is not Non-Conforming Drug Substance but where such Clinical Batch does not satisfy PROTEON's requirements.

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## ARTICLE 11 RECALLS

11.1 Recalls; Quality Agreement. As further set forth in the Quality Agreement, PROTEON shall notify LONZA promptly (and in any event within three (3) Business Days of receipt of written notice) if any Drug Substance or resulting Product is the subject of a recall, market withdrawal, field correction or seizure (a "Recall"). PROTEON shall (i) bear the cost of and be responsible for conducting or responding, to all Recalls of Drug Substance or Product, (ii) remain obligated to pay LONZA in accordance with this Agreement for any Drug Substance used to make such Recalled Product, and (iii) reimburse LONZA for its out-of-pocket expenses related to the Recall, if any. Notwithstanding the foregoing, if such Recall was solely attributable to LONZA's breach of any of its warranties set forth in Section 14.2.1 hereof, upon substantiation of such causation by a mutually agreeable qualified independent arbitrator selected using the procedure specified in Section 10.2, LONZA shall credit or refund PROTEON for the total amount paid by PROTEON to LONZA for the Drug Substance used to make such Recalled Product. Notwithstanding anything to the contrary contained herein, the foregoing obligation shall be LONZA's sole liability and PROTEON's sole remedy under this Agreement with respect to Recalls.

## ARTICLE 12 LICENSE GRANTS

12.1 License to LONZA. During the Term, PROTEON hereby grants to LONZA a fully paid, non-exclusive license under any and all PROTEON Intellectual Property and any Project Intellectual Property owned solely by PROTEON that is necessary for LONZA to perform its obligations under this Agreement, including, without limitation, all rights necessary for the [ ]\* the Manufacturing Process, and/or the PROTEON Confidential Information, for the sole and limited purpose of LONZA's performance of its obligations under this Agreement. For the avoidance of doubt, it is understood that LONZA may not sublicense its rights under this Section 12.1 without PROTEON's prior written consent, which consent shall be provided or denied in accordance with the procedure in Section 4.8.

12.2 License to PROTEON. (a) At the commencement of the development work contemplated by the Project Plan, PROTEON and LONZA shall review the LONZA Intellectual Property that they believe to be relevant to the Project Plan and shall determine which portions of such LONZA Intellectual Property may be useful for the development or manufacturing services contemplated by the Project Plan. The Parties shall agree upon: (i) a listing of the LONZA Intellectual Property to be utilized in such services; (ii) any limitations or restrictions upon the use, development and/or further improvement of such listed LONZA Intellectual Property; and (iii) the one-time fee (if any) applicable to such LONZA Intellectual Property in the event that PROTEON elects to make use of such LONZA Intellectual Property under the circumstances specified in Section 12.2(c), it being understood and agreed that such fee shall not exceed CHF [ ]\* in the aggregate. LONZA shall not incorporate any LONZA Intellectual Property into the Drug Substance, the Product or the Manufacturing Process without the prior written consent of PROTEON. In the event and to the extent that any such

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LONZA Intellectual Property is incorporated into the Drug Substance, the Product or the Manufacturing Process without PROTEON's prior written consent then it shall automatically and without further action by either Party become subject to Section 12.2(b)-(c) on a fully-paid up and royalty-free basis.

(b) LONZA hereby grants to PROTEON a fully paid (subject to compliance with Section 12.2(c) if and when applicable) and royalty-free, non-exclusive, perpetual license, with the right to grant and authorize sublicenses, under any and all LONZA Intellectual Property and Project Intellectual Property owned solely by LONZA that LONZA incorporates into the Manufacturing Process or that is necessary to the practice of the Manufacturing Process or that [ ]\* for the sole and limited purpose of manufacturing Drug Substance and making, having made, using, practicing, offering to sell, selling, importing, exporting and otherwise commercially exploiting Products.

(c) Should PROTEON, after expiration or termination of this Agreement and any and all other agreements that the Parties or their respective Affiliates, successors or assigns enter into for the provision of development or manufacturing services concerning the API, wish to continue to use LONZA Intellectual Property licensed to it under Section 12.2(b) for purposes of having a Third Party contract manufacturer supply it with Drug Substance, then PROTEON shall notify LONZA of its decision and shall pay LONZA the one-time fee agreed upon by the Parties pursuant to Section 12.2(a)(iii).

### ARTICLE 13 OWNERSHIP OF INTELLECTUAL PROPERTY, MATERIALS AND EQUIPMENT

13.1 Intellectual Property. (a) Neither Party will, as a result of this Agreement, acquire any right, title, or interest in any Intellectual Property (including any Confidential Information) of the other Party except as expressly stated under Article 12 or this Article 13.

(b) Project Intellectual Property that relates exclusively to (i) the PROTEON Intellectual Property or (ii) the API, the Drug Substance, the Product, including the development, formulation or manufacture of the API, the Drug Substance or the Product; shall, regardless of inventorship, become the sole property of PROTEON.

(c) Project Intellectual Property that relates exclusively to (i) the LONZA Intellectual Property or (ii) the development, formulation or manufacture of biopharmaceutical products generally, but is not useful to the development, formulation or manufacture of the API, the Drug Substance or the Product, shall, regardless of inventorship, become the sole property of LONZA; provided, that LONZA shall only use such Project Intellectual Property with respect to products that are not elastase products (i.e., any proteinase that possesses the ability to solubilize elastin).

(d) Project Intellectual Property not covered by Section 13.1(b) or Section 13.1(c) shall, regardless of inventorship, be owned jointly by LONZA and PROTEON and will be considered Confidential Information of both Parties; provided, that each Party shall have the right to exploit and license any such jointly owned Intellectual Property without the prior consent of the other Party and without any duty to account to the other Party; provided that (i) PROTEON shall only

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use such Project Intellectual Property with respect to the Product and other elastase products (i.e., any proteinase that possesses the ability to solubilize elastin) and (ii) LONZA shall only use such Project Intellectual Property with respect to products that are not elastase products.

(e) During the term of this Agreement, each Party shall promptly disclose to the other in writing any Project Intellectual Property that might, under applicable law, be patentable or otherwise protectable and the determination of inventorship of such Project Intellectual Property shall be made in accordance with the rules of inventorship of the United States of America. The Parties hereby agree that neither Party shall be considered an "employee or agent" of the other Party. PROTEON shall control the filing, prosecution, maintenance and enforcement of any Patents constituting jointly-owned Project Intellectual Property, at its sole cost and expense, and shall keep LONZA regularly informed with respect to such activities.

(f) Each Party shall sign all necessary documents or take such other actions as may reasonably be requested in order to perfect any and all rights of the applicable Party(ies) in Project Intellectual Property. Each Party will obtain all assignments and agreements necessary from their respective employees and agents and Subcontractors to secure such rights. All costs and expenses for perfecting and enforcing a Party's rights in such Project Intellectual Property, shall be borne by the owner except as otherwise provided in Section 13.1(e).

13.2 PROTEON Materials. As between the Parties, PROTEON shall own all rights in and title to the [ ]\*.

13.3 Ownership of PROTEON Equipment. PROTEON shall own all right, title and interest in and to any and all PROTEON Equipment, as well as all materials and other assets purchased by LONZA, for which the cost is reimbursed by PROTEON to LONZA. PROTEON shall be liable for all damage and risk of loss to the PROTEON Equipment, unless caused by LONZA's negligence or willful misconduct.

13.3.1 PROTEON is responsible for the testing, installation, qualification and validation, as required, of PROTEON Equipment. LONZA will operate and maintain the PROTEON Equipment as per approved procedures once such equipment is commissioned and in operation.

13.3.2 PROTEON shall be liable for repair of all damage and risk of any loss to the PROTEON Equipment, unless caused by LONZA's negligence or willful misconduct.

13.3.3 PROTEON is responsible for any delays to the Project Plan caused in whole or in part by delays in the delivery, testing, qualification or validation of PROTEON Equipment, including any resulting changes in the GMP Suite Activation Date as described in Section 18.2.

### ARTICLE 14 REPRESENTATIONS AND WARRANTIES

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14.1.1 Materials and Information. PROTEON is free to supply to LONZA the [ ]\* PROTEON Confidential Information (including, without limitation, any portion of the Manufacturing Documentation supplied by PROTEON to LONZA), and any other information or materials supplied by PROTEON to LONZA;

14.1.2 No Patent Infringement. No Third Party has filed, pursued or maintained or threatened in writing to file, pursue or maintain any claim, lawsuit, charge, complaint or other action alleging infringement of a Third-Party Patent based on the manufacture, use, import, offer for sale or sale of the Drug Substance or the Product;

14.1.3 No Infringement by Performance of Obligations. To the best of PROTEON's knowledge, PROTEON's supply to LONZA of the [ ]\* and PROTEON Confidential Information (including, without limitation, any portion of the Manufacturing Documentation supplied by PROTEON to LONZA), and any other information or materials that PROTEON intends to supply to LONZA hereunder, and LONZA's use thereof in accordance with the terms of and in performance of its obligations under this Agreement, does not infringe any Third-Party Patent or any other intellectual property rights of any Third Party for which PROTEON lacks the right to grant LONZA a valid sublicense to manufacture the Drug Substance;

14.1.4 No Infringement through Manufacturing Process. To the best of PROTEON's knowledge, the manufacturing process for the Drug Substance in effect as of the Effective Date, as well as any other Manufacturing Process to be provided by PROTEON to LONZA under this Agreement, does not infringe any Third-Party Patent or any other intellectual property rights of any Third Party for which PROTEON lacks the right to grant LONZA a valid sublicense to manufacture the Drug Substance;

14.1.5 No Hazards. PROTEON has made LONZA aware of any known hazards involved in handling the [ ]\*, the Raw Materials, the Drug Substance, and any Wastes generated through performance of the process development and manufacturing activities contemplated hereunder;

14.1.6 License. PROTEON has the right, power and authority to grant LONZA the license set forth in Section 12.1 above and will not enter into any contract, arrangement or commitment in the future which prohibits the grant of such license.

14.1.7 Power and Authority. PROTEON has the corporate power, the authority, the financial capacity and the legal right to enter into this Agreement and to perform its; obligations under this Agreement; and

14.1.8 Execution, Delivery and Performance of the Agreement. PROTEON has taken all necessary corporate action on its part to authorize the execution and delivery of this Agreement and the performance of its obligations under this Agreement. This Agreement has been duly executed and delivered on behalf of PROTEON, and constitutes a legal, valid, binding obligation, enforceable against PROTEON and its successors and assigns in accordance with its terms, except as enforceability may be limited by bankruptcy, fraudulent conveyance, insolvency, reorganization, moratorium and other laws relating to or affecting creditors' rights generally and by general equitable principles. The execution, delivery and performance of this Agreement does not

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breach, violate, contravene or constitute a default under any contracts, arrangements or commitments to which PROTEON is a party or by which it is bound nor does the execution, delivery and performance of this Agreement by PROTEON violate any order, law or regulation of any court, governmental body or administrative or other agency having authority over it.

14.2 LONZA. LONZA hereby represents and warrants to PROTEON that:

14.2.1 Drug Substance. Each Clinical Batch of Drug Substance manufactured hereunder: (i) was manufactured and analyzed in conformance with the Master Production Record; (ii) was manufactured in compliance with the requirements of cGMP; (iii) was packaged in accordance with the Shipping Guidelines; (iv) was transferred free and clear of any liens or encumbrances of any kind to the extent arising through or as a result of the acts or omissions of LONZA; and (v) does not contain any substance that (1) causes such Clinical Batch to be adulterated within the meaning of the U.S. Federal Food, Drug and Cosmetic Act of 1938 and applicable regulations promulgated thereunder, as amended from time to time ("FDCA") or comparable laws or regulations of another government agency or authority that has jurisdiction over the manufacture, testing, distribution, sale or use of Drug Substance or Product, or (2) is present in such Clinical Batch at a level that exceeds the level allowed under the FDCA or comparable laws or regulations of another government agency or authority that has jurisdiction over the manufacture, testing, distribution, sale or use of Drug Substance or Product;

14.2.2 LONZA Facility. LONZA owns or lawfully controls the LONZA Facility, and that the LONZA Facility shall be maintained in accordance with cGMP and in such condition as will allow LONZA to manufacture the Drug Substance in compliance with cGMP and in conformance with the Master Production Record;

14.2.3 Confidential Information. LONZA is free to supply LONZA Confidential Information to PROTEON (excluding any information related to other LONZA clients that PROTEON inadvertently becomes aware of through the presence of its employees or agents at LONZA offices or at the LONZA Facility);

14.2.4 License. LONZA has the right, power and authority to grant PROTEON the license set forth in Section 12.2 above and will not enter into any contract, arrangement or commitment in the future which prohibits the grant of such license.

14.2.5 Power and Authority. LONZA has the corporate power, authority and the legal right to enter into this Agreement and to perform its obligations under this Agreement; and

14.2.6 Execution, Delivery and Performance of Agreement. LONZA has taken all necessary corporate action on its part to authorize the execution and delivery of this Agreement and the performance of its obligations under this Agreement. This Agreement has been duly executed and delivered on behalf of LONZA, and constitutes a legal, valid, binding obligation, enforceable against LONZA in accordance with its terms except as enforceability may be limited by bankruptcy, fraudulent conveyance, insolvency, reorganization, moratorium and other laws relating to or affecting creditors' rights generally and by general equitable principles. The execution, delivery and performance of this Agreement does not breach, violate, contravene or constitute a default under any contracts, arrangements or commitments to which LONZA is a party or by which it is

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bound nor does the execution, delivery and performance of this Agreement by LONZA violate any order, law or regulation of any court, governmental body or administrative or other agency having authority over it.

14.2.7 Performance. LONZA shall use Commercially Reasonable Efforts to develop the Manufacturing Process in a manner that (a) does not infringe any valid and enforceable Patents of any Third Party in the United States or Switzerland, and (b) does not knowingly infringe or misappropriate any other Intellectual Property rights of any Third Party.

14.3 Disclaimer by LONZA.

OTHER THAN AS SET FORTH IN SECTION 14.2, ALL OTHER WARRANTIES, BOTH EXPRESS AND IMPLIED, ARE HEREBY EXPRESSLY DISCLAIMED, INCLUDING, WITHOUT LIMITATION, ANY WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE OF THE DRUG SUBSTANCE OR THE SERVICES PROVIDED HEREUNDER. OTHER THAN THE PROCESS DEVELOPMENT AND MANUFACTURING SERVICES PROVIDED HEREUNDER, LONZA HAS NOT PARTICIPATED IN THE RESEARCH AND DEVELOPMENT OF THE DRUG SUBSTANCE OR THE PRODUCT, NOR HAS LONZA IN ANY WAY EVALUATED THE DRUG SUBSTANCE OR PRODUCT'S SAFETY OR EFFICACY IN HUMANS OR OTHERS.

**ARTICLE 15  
INDEMNIFICATION**

15.1 Indemnification by PROTEON. Subject to and except to the extent of any indemnification from LONZA pursuant to Section 15.2 below, PROTEON shall indemnify, defend and hold LONZA, its Affiliates, and their respective directors, officers, employees and agents harmless from and against all losses, damages, liabilities, settlements, penalties, fines, costs and expenses (including, without limitation, reasonable attorneys' fees and expenses), (collectively, the "Liabilities") to the extent such Liabilities arise out of or result from any claim, lawsuit or other action or threat by a Third Party arising out of (a) the manufacture, packaging, testing, labeling, handling, distribution, marketing, use, import or sale of the Product, in any form, (b) any breach of the representations, warranties and covenants made by PROTEON under this Agreement, (c) PROTEON's negligent acts or omissions or willful misconduct, and/or (d) any Recall of the Product. The foregoing indemnification action shall not apply in the event and to the extent that such Liabilities arise out of or result from any breach of the representations, warranties and covenants made by LONZA under this Agreement, or LONZA's negligent acts or omissions or willful misconduct.

15.2 Indemnification by LONZA. Subject to and except to the extent of any indemnification from PROTEON pursuant to Section 15.1 above, LONZA shall indemnify, defend and hold PROTEON, and its Affiliates, directors, officers, employees and agents harmless from and against all Liabilities to the extent such Liabilities arise out of or result from any claim, lawsuit or other action or threat by a Third Party arising out of (a) any breach of the representations, warranties and covenants made by LONZA under this Agreement, or (b) LONZA's negligent acts or omissions or willful misconduct.

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15.3 Indemnification Procedures.

15.3.1 Identification of Indemnitor and Indemnitee. An "Indemnitor" means the indemnifying Party. An "Indemnitee" means the indemnified Party, its Affiliates, and their respective directors, officers, employees and agents.

15.3.2 Indemnification Procedures. To receive the benefit of indemnification under Section 15.1 or Section 15.2, an Indemnitee which intends to claim indemnification under Section 15.1 or Section 15.2 hereof must (a) promptly notify the Indemnitor in writing of any claim, lawsuit or other action in respect of which the Indemnitee intend to claim such indemnification; provided, that failure to give such notice shall not relieve Indemnifying Party of its indemnification obligations except where, and solely to the extent that, such failure actually and materially prejudices the lights of Indemnifying Party; (b) tender to the Indemnitor, and cause its Affiliates and their respective directors, officers, employees and agents to tender to, the Indemnitor, full authority to defend or settle the claim or suit; at its discretion, to provided that no settlement requiring any admission by the Indemnitee or that imposes any obligation on the Indemnitee shall be made without the Indemnitee's consent; and (c) provide reasonable cooperation to the Indemnitor and its legal representatives and insurer, and cause its Affiliates and their respective directors, officers, employees and agents to reasonably cooperate with the Indemnitor and its legal representatives and insurer in the investigation and defense of any claim, lawsuit or other action covered by this indemnification, as reasonably requested, at Indemnitor's cost and expense. Neither Party, as an Indemnitor, shall have any obligation to indemnify the Indemnitee in connection with any settlement made without the prior written consent of the Indemnitor and the Indemnitor shall not be responsible for any legal fees or other costs incurred other than as provided herein. The Indemnitee shall have the right, but not the obligation, to be represented by counsel of its own selection and at its sole expense.

15.4 Insurance. PROTEON shall maintain commercial general liability insurance including product liability insurance with respect to development, manufacture, import, sale, offer for sale and use of the Drug Substance and/or Products by PROTEON and its Affiliates in a minimum amount of [ ]\* per occurrence (not including any self-insured retention). PROTEON will maintain such insurance policy with an insurance company having a minimum AM Best rating of A and that is licensed to do business in the Commonwealth of Massachusetts. PROTEON will provide LONZA with at least thirty (30) days' written notice prior to non-renewal, termination, or modification of coverage. LONZA shall maintain commercial general liability insurance with respect to its activities under this Agreement in a minimum amount of [ ]\* per occurrence (not including any self-insured retention). LONZA shall maintain such insurance during the Term and for a period of three (3) years thereafter. LONZA will maintain such insurance policy with an insurance company having a minimum AM Best rating of A and that is licensed to do business in the Commonwealth of Massachusetts. LONZA will provide PROTEON with at least thirty (30) days' written notice prior to non-renewal, termination, or modification of coverage.

15.5 Disclaimer of Consequential Damages. EXCEPT FOR BREACH OF CONFIDENTIALITY OBLIGATIONS UNDER ARTICLE 16 AND EXCEPT AS OTHERWISE PROVIDED IN SECTIONS 15.1 AND 15.2 WITH RESPECT TO THIRD

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PARTY CLAIMS, IN NO EVENT SHALL EITHER PARTY BE LIABLE TO THE OTHER OR ANY OF ITS AFFILIATES FOR ANY CONSEQUENTIAL, INCIDENTAL, INDIRECT, SPECIAL, PUNITIVE OR EXEMPLARY DAMAGES (INCLUDING, WITHOUT LIMITATION, LOST PROFITS, BUSINESS OR GOODWILL) SUFFERED OR INCURRED BY SUCH OTHER PARTY OR ITS AFFILIATES IN CONNECTION WITH THIS AGREEMENT, EVEN IF ADVISED OF THE POSSIBILITY OF SUCH DAMAGES.

15.6 Disclaimer regarding Transfer and Engineering Runs. PROTEON shall have the right to make whatever further use of the Transfer and/or Engineering Batches as it shall determine, provided that such use does not violate any applicable laws, rules or regulations. LONZA SHALL IN NO WAY BE RESPONSIBLE FOR ANY CLAIMS, DEMANDS, LOSSES, LIABILITIES, EXPENSES OR DAMAGES, WHATSOEVER, ARISING OUT OF OR IN ANYWAY RELATED TO PROTEON'S USE OF SUCH TRANSFER BATCHES AND/OR ENGINEERING BATCHES.

15.7 Limitation of Liability. BOTH PARTIES HEREBY AGREE THAT TO THE FULLEST EXTENT PERMITTED BY LAW, AND EXCEPT FOR BREACH OF CONFIDENTIALITY OBLIGATIONS UNDER ARTICLE 16 AND EXCEPT AS OTHERWISE PROVIDED IN SECTIONS 15.1 AND 15.2 WITH RESPECT TO THIRD PARTY CLAIMS, EACH PARTY'S LIABILITY TO THE OTHER, FOR ANY AND ALL INJURIES, CLAIMS, LOSSES, EXPENSES, OR DAMAGES, WHATSOEVER, ARISING OUT OF OR IN ANY WAY RELATED TO THIS AGREEMENT FROM ANY CAUSE OR CAUSES, INCLUDING, BUT NOT LIMITED TO, NEGLIGENCE, ERRORS, OMISSIONS OR STRICT LIABILITY, SHALL NOT EXCEED THE TOTAL CHARGES PAID OR PAYABLE BY PROTEON TO LONZA UNDER THIS AGREEMENT. TO THE EXTENT THAT THIS CLAUSE CONFLICTS WITH ANY OTHER CLAUSE, THIS CLAUSE SHALL TAKE PRECEDENCE OVER SUCH CONFLICTING CLAUSE. IF APPLICABLE LAW PREVENTS ENFORCEMENT OF THIS CLAUSE, THEN THIS CLAUSE SHALL BE DEEMED MODIFIED TO PROVIDE THE MAXIMUM PROTECTION FOR EACH PARTY AS IS ALLOWABLE UNDER APPLICABLE LAW.

## ARTICLE 16 CONFIDENTIALITY

16.1 LONZA Confidentiality Obligations. LONZA shall not use PROTEON Confidential Information except as authorized under this Agreement and shall not disclose PROTEON Confidential Information to any Third Party other than: (i) employees, consultants, agents or Subcontractors of LONZA or LONZA's Affiliates who are bound by similar obligations of confidentiality and nonuse and who have a need to know such information in order to perform their duties or services in connection with LONZA's obligations under this Agreement; (ii) Regulatory Authorities that require such information in connection with making Regulatory Filings and maintaining Regulatory Authority approvals for the Product, provided that reasonable effort will be taken to ensure confidential treatment of such information; (iii) Governmental Authorities in connection with securing and maintaining Registrations, provided that reasonable effort will be taken to ensure confidential treatment of such information; (iv) in response to a valid order or subpoena of a court of competent

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jurisdiction or other governmental body of a country or any political subdivision thereof of competent jurisdiction, provided that LONZA provides PROTEON with prior written notice of such disclosure (if practicable) in order to permit PROTEON to seek a protective order or other confidential treatment of such PROTEON Confidential Information, provided further that any PROTEON Confidential Information so disclosed will be limited to that information that is legally required to be disclosed in such response to such court or governmental order or subpoena; (v) as otherwise required by applicable law or regulation, provided that LONZA provides PROTEON with prior written notice of such disclosure (if practicable) in order to permit PROTEON to seek a protective order or confidential treatment of such PROTEON Confidential Information, provided further that any PROTEON Confidential Information so disclosed will be limited to that information that is legally required by applicable law to be disclosed; or (vi) Swiss or foreign tax authority to the extent legally required by applicable law to be disclosed.

16.2 PROTEON Confidentiality Obligations. PROTEON shall not use LONZA Confidential Information except as authorized under this Agreement and shall not disclose any LONZA Confidential Information to any Third Party other than: (i) employees, consultants, or agents of PROTEON or PROTEON's Affiliates who are bound by similar obligations of confidentiality and nonuse and who have a need to know such information in order to perform their duties or services in connection with PROTEON's obligations under this Agreement or the development or commercialization of the Product; (ii) Regulatory Authorities that require such information in connection with making Regulatory Filings and maintaining Regulatory Authority approvals for the Product, provided that reasonable effort will be taken to ensure confidential treatment of such information; (iii) Governmental Authorities in connection with securing and maintaining Registrations, provided that reasonable effort will be taken to ensure confidential treatment of such information; (iv) to sublicensees in connection with the exercise of the license granted to PROTEON under Article 12; (v) in response to a valid order or subpoena of a court of competent jurisdiction or other governmental body of a country or any political subdivision thereof of competent jurisdiction, provided that PROTEON provides LONZA with prior written notice of such disclosure (if practicable) in order to permit LONZA to seek a protective order or other confidential treatment of such LONZA Confidential Information, provided further that any LONZA Confidential Information so disclosed will be limited to that information that is legally required to be disclosed in such response to such court or governmental order or subpoena; (vi) as otherwise required by applicable law or regulation, provided that PROTEON provides LONZA with prior written notice of such disclosure (if practicable) in order to permit LONZA to seek a protective order or confidential treatment of such LONZA Confidential Information, provided further that any LONZA Confidential Information so disclosed will be limited to that information that is legally required by applicable law to be disclosed; or (vii) to U.S. or foreign tax authority to the extent legally required by applicable law to be disclosed.

16.3 Responsibility for Compliance with Confidentiality and Nonuse Obligations. Each Party shall be responsible for any misuse or misappropriation, by such Party, its Affiliates, or the employees, consultants, agents, Subcontractors or sublicensees of such Party or such Party's Affiliates, of the other Party's Confidential Information.

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16.4 Terms of Agreement. Neither Party shall, without the prior written consent of the other Party, disclose in any manner to any Third Party the terms and conditions of this Agreement.

16.5 Exclusions. The obligations of confidentiality and nonuse set forth in Section 16.1 and Section 16.2 and Section 16.4 shall not apply to any information that: (i) is released with the prior written consent of the disclosing Party; (ii) is required to comply with national, federal or state laws, rules or regulations (including the rules and regulations of any national stock exchange on which such Party's securities are traded), provided that the receiving Party promptly notifies the disclosing Party of such required disclosure, takes all reasonable and lawful actions to obtain confidential treatment of such disclosure and furnishes only that portion of the Confidential Information which is legally required to be disclosed; or (iii) is disclosed to a Party's employees, consultants, agents, Subcontractors, sublicensees, potential acquirers, investors or potential investors, on a need-to-know basis, under reasonable conditions of confidentiality. In determining whether or not the disclosing Party's Confidential Information has entered the public domain, the obligations of confidentiality shall no longer apply to only that portion of said Confidential Information that has become public, and portions remaining confidential shall retain their status as Confidential Information. Each Party shall notify the other promptly on discovery of any unauthorized use or disclosure of the other Party's trade secrets or proprietary information.

16.6 No Licenses. Except as expressly provided in Article 12 hereof, no right or license, either express or implied, is granted under any intellectual property right or by virtue of the disclosure of Confidential Information under this Agreement, or otherwise.

16.7 Maintenance of Confidentiality. Each Party shall use reasonable and customary precautions to safeguard the other Party's Confidential Information, including ensuring that all employees, consultants, agents, Subcontractors or sublicensees who are provided access to such Confidential Information are informed of the confidential and proprietary nature of such Confidential Information and have contractual confidentiality and nonuse obligations that are at least as restrictive as those contained in this Agreement.

16.8 Termination of Certain Prior Agreements. This Agreement supersedes in its entirety the Confidentiality Agreement. All Confidential Information (as defined in such Confidentiality Agreement) exchanged between the Parties under such agreement shall be deemed Confidential Information under this Agreement (either PROTEON Confidential Information or LONZA Confidential Information, as the context requires) and shall be subject to the terms of this Agreement from and after the Effective Date, but shall remain subject to the Confidentiality Agreement with respect to the period prior to the Effective Date.

16.9 No Disclosure of Unrelated Information. Neither Party shall disclose Confidential Information to the other Party that is not reasonably necessary for performance of a Party's obligations under this Agreement, including but not limited to manufacturing processes for other products, marketing plans and clinical development plans. Notwithstanding the foregoing, nothing in this provision shall limit the confidentiality and non-use obligations and rights in this Article 16.

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**ARTICLE 17  
PRESS RELEASES; USE OF NAMES**

17.1 **Press Releases.** The Parties agree that any initial public announcement of the execution of this Agreement shall be in the form of a mutual press release to be agreed upon by the Parties; provided, that the Parties shall also agree on the timing of such public announcement. After such press release is published, each Party shall be entitled to make or publish any public statement consistent with the contents thereof. Except as set forth in the preceding sentence, no press release, publicity or other form of public written disclosure related to this Agreement shall be permitted by either Party unless the other Party has indicated its consent to the form of the release in writing. This Section 17.1 shall not apply to any disclosure that is deemed necessary, in the reasonable judgment of the responsible Party, to comply with national, federal or state laws or regulations (including the rules and regulations of any national stock exchange on which such Party's securities are traded).

17.2 **Use of Names.** Neither Party shall make use of the name of the other Party in any advertising or promotional material, or otherwise, in connection with this Agreement or any related agreements, without the prior written consent of such other Party.

**ARTICLE 18  
TERM; TERMINATION**

18.1 **Term; Option to Extend.** Unless sooner terminated pursuant to the terms of this Agreement, the term of this Agreement shall commence on the Effective Date and shall continue until the later of (i) the third (3<sup>rd</sup>) anniversary of the Effective Date and (ii) the completion of all deliverables contemplated by the Project Plan and Exhibit B (such period during which this Agreement is in effect, the "Term"). The Parties may, by written agreement, extend the Term of this Agreement for an additional period of time.

18.2 **Scheduling and Rescheduling.** The initial scheduling of LONZA production activities is set forth in the Project Plan. The Project Plan includes the "Suite Activation Date" ("Suite Activation Date") which locks the target date for occupancy of this Project in the designated LONZA GMP suite or suites and dedicates LONZA resources and assets to meeting that date. If PROTEON requests to change the Suite Activation Date, LONZA will make all reasonable attempts to accommodate the request. In the event that this change would impact other projects scheduled for occupancy in the designated suite or suites, PROTEON's Project may be delayed until an adequate time period is available in the schedule for the designated LONZA suite or suites and dedicated resources.

18.3 **Batch Cancellation.** Stage 3 as described in the Project Plan may be cancelled by PROTEON upon written notification to LONZA (effective upon date of receipt by LONZA) under the following schedule and cancellation fees:

18.3.1 Cancellation for Convenience: The cancellation fee shall be a percentage of the total Stage 3 Price (where the total Stage 3 price is CHF [ ]\* or as agreed otherwise in a Change Order), less any sums already received under the Project Plan in respect of Stage 3 at the time the cancellation fee is calculated. The applicable percentage shall be dependent on the period

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of time between (i) notice of cancellation and (ii) the then current date for Suite Activation Date of Stage 3 as follows:

<i>Period prior to Suite Activation Date of Stage 3</i>	<i>Percentage of Stage 3 Price</i>
[ ]* months from Suite Activation Date	[ ]*
[ ]* from Suite Activation Date	[ ]*
[ ]* months from Suite Activation Date	[ ]*

18.3.2 Cancellation for Cause (i.e. clinical failure, regulatory hold, a LONZA generated or Change Order-generated Project delay(s) during Stage 1 and/or 2 of the Project Plan which result(s) in unacceptable delay(s) to the Suite Activation Date, or the like) but specifically excluding events that would permit PROTEON to terminate this Agreement pursuant to Section 18.4. The cancellation fee shall be a percentage of the total Stage 3 Price (where the total Stage 3 price is CHF [ ]\*, or as agreed otherwise in a Change Order), less any sums already received under the Project Plan in respect of Stage 3 at the time the cancellation fee is calculated. The applicable percentage shall be dependent on the period of time between (i) notice of cancellation and (ii) the then current date for Suite Activation Date of Stage 3 as follows:

<i>Period prior to Suite Activation Date of Stage 3</i>	<i>Percentage of Stage 3 Price</i>
[ ]* months from Suite Activation Date	[ ]*

18.3.3 Notwithstanding the foregoing, LONZA will use Commercially Reasonable Efforts to manufacture alternate product in the Facility for PROTEON or, if PROTEON does not so request, for a third party, in order to mitigate any financial loss suffered by LONZA or PROTEON due to the Batch Cancellation by PROTEON or a designated Affiliate of PROTEON. Should LONZA be able to manufacture alternate product for PROTEON or a third party, then the applicable cancellation fee set forth in Section 18.3.1 and 18.3.2 shall be waived and PROTEON shall not be obligated to pay any such fee, or if such fee has been previously paid by PROTEON shall be refunded by LONZA.

18.3.4 Any amounts payable in 18.3.1 and 18.3.2 shall be due within thirty (30) days of the receipt of invoice.

18.4 Termination. This Agreement may be terminated as follows:

18.4.1 Material Breach. Either Party may terminate this Agreement, by written notice to the other Party, for any material breach of this Agreement by the other Party, if such breach is not cured within thirty (30) days after the breaching Party receives written notice of such breach from the non-breaching Party; provided, however, that if such breach is not capable of being

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cured within such thirty-day period and the breaching Party has commenced and diligently continued actions to cure such breach within such thirty-day period, except in the case of a payment default, the cure period shall be extended to sixty (60) days, so long as the breaching Party is making diligent efforts to do so. Such termination shall be effective upon expiration of the applicable cure period.

18.4.2 Force Majeure Termination. The “disadvantaged” Party shall have the right to terminate this Agreement, upon providing written notice thereof to the other Party, such termination to be effective thirty (30) days from the date of such notice under the conditions set forth in Section 19.1.

18.4.3 Insolvency. Either Party may terminate this Agreement upon notice to the other Party, upon (a) the dissolution, termination of existence, liquidation or business failure of the other Party; (b) the appointment of a custodian or receiver for the other Party who has not been terminated or dismissed within ninety (90) days of such appointment; (c) the institution by the other Party of any proceeding under national, federal or state bankruptcy, reorganization, receivership or other similar laws affecting the rights of creditors generally or the making by such Party of a composition or any assignment for the benefit of creditors under any national, federal or state bankruptcy, reorganization, receivership or other similar law affecting the rights of creditors generally, which proceeding is not dismissed within ninety (90) days of filing. All rights and licenses granted pursuant to this Agreement are, and shall otherwise be deemed to be, for purposes of Section 365(n) of Title 11 of the United States Code, licenses of rights of “intellectual property” as defined therein.

18.4.4 Failure to Establish the Manufacturing Process. This Agreement may be terminated in its entirety by PROTEON in the event that LONZA is unable to develop a Manufacturing Process in accordance with Project Plan that meets the [ ]\* specified in Exhibit D to this Agreement, despite the use of Commercially Reasonable Efforts to do so. In the event of such termination, PROTEON’s liability shall be limited to the Project costs actually incurred by LONZA prior to the effective date of termination. In addition, the Agreement may be terminated in its entirety by LONZA upon completion of Stage 2 of the Project Plan or thereafter should LONZA determine, in good faith, that the Manufacturing Process is not suitable for implementation in the cGMP Facility after Commercially Reasonable Efforts to establish the Manufacturing Process have been completed. In the event of such termination, PROTEON’s liability shall be limited to the Project costs actually incurred by LONZA prior to the effective date of termination. PROTEON shall not be liable under this Clause 18.4.4 to pay to LONZA in aggregate a sum in excess of the amount set forth in the Project Plan (plus LONZA-incurred Acquisition Costs), as may be amended from time-to-time pursuant to Section 3.4, for the completed, or partially completed, stages or sub-stages of the Project at the time of such termination.

18.4.5 Cumulative Remedies. Any right to terminate this Agreement shall be in addition to and not in lieu of all other rights or remedies that the Party giving notice of termination may have at law or in equity or otherwise.

18.5 Consequences of Termination.

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18.5.1 Payment of Amounts Due. Expiration or termination of this Agreement for any reason shall not exempt either Party from paying to the other Party any amounts owing to such Party at the time of such expiration or termination.

18.5.2 **This Section Intentionally Omitted.**

18.5.3 Termination of Runs. Runs that are in process as of the effective date of any termination hereunder shall not be cancelled without the mutual agreement of the Parties, and the Agreement shall continue to survive with respect to those in-process Runs. Drug Substance that has been fully manufactured as of the date of such termination, but for which Quality Review and Approval has not been completed, shall remain subject to the terms of this Agreement, and the Agreement shall continue to survive with respect to such Drug Substance.

18.5.4 Raw Materials, Consumables and Resins. Upon expiration or termination of this Agreement, PROTEON shall purchase from LONZA (to the extent not previously purchased), at LONZA’s Acquisition Cost, all remaining usable Raw Materials, Consumables and Resins acquired and paid for by LONZA for the manufacture of Drug Substance under this Agreement, provided that such Raw Materials, Consumables and Resins are in resalable condition and provided, that as of the date of receipt of the termination notice, LONZA shall place no further orders for Raw Materials, Consumables and Resins except as may be necessary for completion of any portion of LONZA’s services hereunder that are not immediately terminated.

18.5.5 Return of Materials and of PROTEON Confidential Information; Transfer of PROTEON Equipment. Upon expiration or termination of this Agreement, unless otherwise directed by PROTEON, LONZA shall promptly at PROTEON’s sole cost and expense (i) return or, at PROTEON’s election, destroy, all quantities of the [ ]\* received by LONZA under this Agreement, (ii) return all PROTEON Confidential Information to PROTEON, except for a single copy and/or sample which may be retained for documentation purposes only and which shall remain subject to the obligations of nonuse and confidentiality set forth

in this Agreement, (iii) deliver to PROTEON all Reference Materials (except that LONZA shall have the right to keep a retain sample of each Reference Material) being held by LONZA, and (iv) deliver all remaining Raw Materials, Consumables and Resins purchased pursuant to Section 18.5.4. In addition, LONZA shall transfer all PROTEON Equipment to PROTEON, at PROTEON's sole cost and expense, within sixty (60) days of expiration or termination of this Agreement. If any PROTEON owned property (PROTEON Equipment, Drug Substance, Raw Materials, etc.) remains at the LONZA Facility for a period longer than ninety (90) days after expiration or termination of this Agreement, PROTEON shall pay for such storage as Additional Services in accordance with the applicable Project Rates. Any deliveries made pursuant to Section 18.4 shall be made FCA the LONZA Facility.

18.5.6 Return of LONZA Confidential Information. Upon expiration or termination of this Agreement, PROTEON shall promptly return all LONZA Confidential Information to LONZA, except for a single copy which may be retained for documentation purposes only and which shall remain subject to the obligations of nonuse and confidentiality set forth in this Agreement.

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18.5.7 Accrued Rights. Except as otherwise expressly set forth herein, any termination or expiration of this Agreement shall be without prejudice to any right which shall have accrued to the benefit of either Party and shall not relieve either Party of any obligation which has accrued prior to the effective date of such termination or expiration, which obligations shall remain in full force and effect for the period provided therein or, if no period is provided therein, then such obligations shall remain in full force and effect indefinitely.

18.6 Surviving Rights. Article 1, Section 4.7 (only with respect to hazards that may exist or handling of materials which may take place after the termination date), Article 5 (only with respect to work in progress as of the termination date), Article 6 (only with respect to invoices unpaid as of the termination date or issued thereafter for work in progress as of the termination date), Article 10, Article 11, Article 12, Article 13, Article 15, Article 16, Article 17, Section 18.4, Section 18.5, Section 18.6, and Article 20, and the rights and obligations contained therein, shall survive the termination or expiration of this Agreement.

#### ARTICLE 19 FORCE MAJEURE

19.1 Effects of Force Majeure. Except as otherwise provided in this Agreement, in the event that a delay or failure of a Party to comply with any obligation created by this Agreement (except for payment of any amounts due under this Agreement) if such failure is caused by an act of God, fire, flood, act of government or state, war, civil commotion, insurrection, acts of terrorism, embargo, sabotage, a viral, bacterial or Mycoplasmal contamination which causes a shutdown of the LONZA Facility, prevention from or hindrance in obtaining energy or other utilities, a shortage of Raw Materials, Resins, Consumables or other necessary components, labor disputes of whatever nature, or any other reason beyond the control and without the fault or negligence of the Party affected thereby (collectively, a "Force Majeure Event"), the "affected Party" will, after giving prompt notice to the "disadvantaged Party" in accordance with Section 19.2, be excused from such performance on a day-to-day basis during the continuance of such Force Majeure Event continues (and the disadvantaged Party will likewise be excused from performance of its obligations on a day-to-day basis during the same period); provided that upon cessation of such Force Majeure Event, the affected Party shall promptly resume performance under this Agreement. If Force Majeure Event conditions continue for more than ninety (90) consecutive days or an aggregate one hundred eighty (180) days in any 12-month period, then the "disadvantaged" Party may terminate this Agreement in accordance with Section 18.4.2.

19.2 Notice of Force Majeure. Each Party agrees to give the other Party prompt written notice of the occurrence of any Force Majeure Event, the nature thereof, and the extent to which the affected Party will be unable to fully perform its obligations under this Agreement. Each "affected" Party further agrees to use its best efforts to correct the Force Majeure Event as quickly as practicable and to give the other Party prompt written notice when it is again fully able to perform such obligations.

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#### ARTICLE 20 MISCELLANEOUS

20.1 Notices. Any notice required or permitted to be given under this Agreement by any Party shall be in writing and shall be (a) delivered personally, (b) sent by registered mail, return receipt requested, postage prepaid, (c) sent by a nationally-recognized courier service guaranteeing next-day or second day delivery, charges prepaid, (d) delivered by facsimile (with documented evidence of transmission), or (e) delivered by electronic mail (with respect to exchanges regarding the Project Plan and proposed Decision Requests or Change Orders or Change Requests and upon documented evidence of receipt, which shall consist of an acknowledgement from the recipient Party that such email transmission has been received) to the addresses or facsimile numbers or email addresses of the other Party set forth below, or at such other addresses as may from time to time be furnished by similar notice by any Party. The effective date of any notice under this Agreement shall be the date of receipt by the receiving Party.

If to LONZA:  
Lonza Ltd  
Attn: Group General Counsel  
Muenchensteinerstrasse 38

If to PROTEON:

Proteon Therapeutics, Inc.  
200 West Street  
Waltham, MA 02451  
Fax: 781-487-6729  
Attn: Mark Fitzpatrick, Chief Financial Officer

20.2 Applicable Law. This Agreement shall be construed, interpreted and enforced in accordance with the internal substantive laws of New York, USA, without reference to the choice of law doctrine of such state that would result in the application of the substantive law of any other jurisdiction. The United Nations Convention on Contracts for the International Sale of Goods shall not apply to this Agreement or the transactions contemplated by this Agreement.

20.3 Dispute Resolution. (a) The Parties will attempt to settle any claim or controversy arising out of this Agreement or the subject matter hereof through consultation and negotiation in good faith in a spirit of mutual cooperation. Such matters will be initially addressed by the Project Managers, who shall use reasonable efforts to attempt to resolve the dispute through good faith negotiations by telephone or in person as may be agreed. If they fail to resolve the dispute within thirty (30) days after either Party notifies the other of the dispute, then the matter will be escalated to the Chief Executive Officer of PROTEON and the

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Chief Executive Officer of LONZA, or their designees for resolution. They will use reasonable efforts to attempt to resolve the dispute through good faith negotiations by telephone or in person as may be agreed. If they fail to resolve the dispute within thirty (30) days after it is referred to them and do not mutually agree to extend the time for negotiation, then the dispute will be submitted to arbitration in accordance with the procedure set forth in Section 20.3(b).

(b) Except with respect to actions by either Party seeking equitable or declaratory relief, any claim or controversy arising in whole or in part under or in connection with this Agreement or the subject matter hereof that is not resolved pursuant to Section 20.3(a) will be referred to and finally resolved by arbitration in accordance with the Rules of the International Chamber of Commerce (the "Rules") as such Rules may be modified by this Agreement, by one arbitrator, who will be agreed upon by the Parties. If the Parties are unable to agree upon a single arbitrator within thirty (30) days following the date arbitration is demanded, three arbitrators will be used, one selected by each Party within ten (10) days after the conclusion of the 30-day period and a third selected by the first two within ten (10) days thereafter. Unless the Parties agree otherwise, they will be limited in their discovery to directly relevant documents. Responses or objections to a document request will be served twenty (20) days after receipt of the request. The arbitrator(s) will resolve any discovery disputes. Arbitration proceedings may be commenced by either Party by notice to the other Party. Unless otherwise agreed by the Parties, all such arbitration proceedings will be held in New York, USA, provided that proceedings may be conducted by telephone conference call with the consent of the Parties and the arbitrator(s). The arbitrator(s) will apply the laws of New York and it is understood and agreed that the provisions of Sections 45 and 69 of the Arbitration Act of 1969 shall not apply in respect of any arbitration pursuant to this Agreement. The arbitrator(s) will only have the authority to award actual money damages (with interest on unpaid amounts from the date due) and, except with respect to a breach or nonperformance of any provision of this Agreement relating to Confidential Information, the arbitrator(s) will not have the authority to award indirect, incidental, consequential, exemplary, special or punitive damages, and the Parties expressly waive any claimed right to such damages. The arbitrator(s) also shall be authorized to grant any temporary, preliminary or permanent equitable remedy or relief the arbitrators deem just and equitable and within the scope of this Agreement, including an injunction or order for specific performance. The award of the arbitrator(s) shall be the sole and exclusive remedy of the Parties. Judgment on the award rendered by the arbitrator(s) may be enforced in any court having competent jurisdiction thereof, subject only to revocation on grounds of fraud or clear bias on the part of the arbitrator(s). The arbitration will be of each Party's individual claims only, and no claim of any other Party will be subject to arbitration in such proceeding. The costs and expenses of the arbitration, but not the costs and expenses of the Parties, will be shared equally by the Parties. If a Party fails to proceed with arbitration, unsuccessfully challenges the arbitration award, or fails to comply with the arbitration award, the other Party is entitled to costs, including reasonable attorneys' fees, for having to compel arbitration or defend or enforce the award. Except as otherwise required by law, the Parties and the arbitrator(s) will maintain as confidential all information or documents obtained during the arbitration process, including the resolution of the dispute. Judgment on the award granted in any arbitration hereunder may be entered in any court having jurisdiction over the award or any of the Parties or any of their respective assets. The Parties knowingly and

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\* CONFIDENTIAL TREATMENT REQUESTED. OMITTED PORTIONS FILED WITH THE SECURITIES AND EXCHANGE COMMISSION PURSUANT TO RULE 406 PROMULGATED UNDER THE SECURITIES ACT OF 1933, AS AMENDED.

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voluntarily waive their rights to have their dispute tried and adjudicated by a judge and jury except as expressly provided herein.

(c) Nothing in this Section 20.3 will prevent a Party from resorting to judicial proceedings if: (i) interim relief from a court is necessary to prevent serious and irreparable injury to such Party; or (ii) litigation is required to be filed prior to the running of the applicable statute of limitations. The use of any alternative dispute resolution procedure will not be construed under the doctrine of laches, waiver or estoppel to affect adversely the rights of either Party.

20.4 Headings. All headings in this Agreement are for convenience of reference only and shall not affect the interpretation of this Agreement.

20.5 Exhibits. All exhibits or appendices referred to herein form an integral part of this Agreement and are incorporated into this Agreement by such reference.

20.6 Security Procedures. All PROTEON personnel visiting or having access to the LONZA Facility shall agree in writing to abide by LONZA standard policies, operating procedures and security procedures as established by LONZA and communicated to PROTEON.

20.7 Assignment. This Agreement shall be binding upon the successors and assigns of the Parties and the name of a Party appearing herein shall be deemed to include the names of its successors and assigns. Neither Party may assign its rights or delegate its duties under this Agreement without the prior written consent of the other Party; provided that either party may assign this Agreement without the consent of the other party to (i) an Affiliate or (ii) in connection with the sale or transfer or other assignment of all or substantially all of the assets of such Party or the line of business or Product to which this Agreement relates, or (iii) in connection with a merger, consolidation, acquisition or other form of business combination; provided, further, that in each instance the assignee expressly assumes all obligations imposed on the assigning Party by this Agreement in writing and the other Party is notified in advance of such assignment. Any purported assignment without a required consent shall be void. No assignment shall relieve any Party of responsibility for the performance of any obligation that accrued prior to the effective date of such assignment.

20.8 Severability. If any part of this Agreement shall be found to be invalid or unenforceable under applicable law in any jurisdiction, such part shall be ineffective only to the extent of such invalidity or unenforceability in such jurisdiction, without in any way affecting the remaining parts of this Agreement in that jurisdiction or the validity or enforceability of the Agreement as a whole in any other jurisdiction. In addition, the part that is ineffective shall be reformed in a mutually agreeable manner so as to as nearly approximate the intent of the Parties as possible.

20.9 Independent Contractors. Each of the Parties is an independent contractor and nothing herein contained shall be deemed to constitute the relationship of partners, joint venturers, nor of principal and agent between the Parties. Neither Party shall at any time enter

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into, incur, or hold itself out to Third Parties as having authority to enter into or incur, on behalf of the other Party, any commitment, expense, or liability whatsoever.

20.10 Waiver. No waiver of any term, provision or condition of this Agreement whether by conduct or otherwise in any one or more instances shall be deemed to be or construed as a further or continuing waiver of any such term, provision or condition or of any other term, provision or condition of this Agreement.

20.11 Counterparts. This Agreement and any amendment hereto may be executed in any number of counterparts, each of which shall for all purposes be deemed an original and all of which shall constitute the same instrument. This Agreement shall be effective upon full execution by facsimile or original, and a facsimile signature shall be deemed to be and shall be as effective as an original signature.

20.12 No Solicitation of Employees. During the Term and for two (2) years thereafter, each of the Parties agrees not to seek to induce or solicit any employee of the other Party or its Affiliates to discontinue his or her employment with the other Party or such Affiliate in order to become an employee or an independent contractor of the soliciting Party or its Affiliates; provided, however, that neither Party shall be in violation of this Section as a result of making a general solicitation for employees or independent contractors. For the avoidance of doubt, the publication of an advertisement shall not constitute solicitation or inducement.

20.13 Entirety; Amendments. This Agreement, including any exhibits attached hereto and referenced herein, and the Quality Agreement constitute the full understanding of the Parties and a complete and exclusive statement of the terms of their agreement with respect to the specific subject matter hereof, and no terms, conditions, understandings or agreements purporting to modify or vary the terms thereof shall be binding unless hereafter made in a written instrument referencing this Agreement and signed by each of the Parties.

20.14 Preference. The terms of this Agreement shall prevail in the event of a conflict between this Agreement and any exhibits or appendices.

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IN WITNESS WHEREOF, each Party hereto has caused this Agreement to be executed on its behalf by its duly authorized representative.

PROTEON THERAPEUTICS, INC.

By: /s/ Timothy Noyes

Name: Timothy Noyes

Title: President & CEO

**LONZA LTD**

By: /s/ Dr. Hans Peter Pfirter

Name: Dr. Hans Peter Pfirter

Title: General Counsel

By: /s/ Thomas Keppler

Name: Thomas Keppler

Title: Head of Patient Department

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\* CONFIDENTIAL TREATMENT REQUESTED. OMITTED PORTIONS FILED WITH THE SECURITIES AND EXCHANGE COMMISSION PURSUANT TO RULE 406 PROMULGATED UNDER THE SECURITIES ACT OF 1933, AS AMENDED.

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**ASSIGNMENT OF RIGHTS/LICENSE AGREEMENT**  
**NIH Sponsored Invention**

This Agreement, effective this 4th day of February 2002, is between the Johns Hopkins University, a corporation of the State of Maryland, having a principle place of business at 720 Rutland Avenue, Baltimore, Maryland 21205 (hereinafter referred to as "JHU") and F. Nicholas Franano, an individual, residing at 1010 W. 69th Terrace, Kansas City, MO 64113 (hereinafter referred to as "FRANANO").

WITNESSETH:

WHEREAS, a valuable invention entitled "Local, Transcatheter Delivery of Proteases to Reopen Obstructed Biological Conduits" JHU Ref. No. DM-3578 (hereinafter Invention) was developed during the course of research conducted by FRANANO, and is disclosed and/or claimed in U.S. Provisional Patent Application Serial No. 60,155,938 filed on September 24, 1999, U.S. Patent Application Serial No 09,669,051 filed on September 24, 2000 and International PCT Application Serial No. PCT/US00/26237 filed on September 24, 2000 (hereinafter Patent Rights); and

WHEREAS, JHU has acquired through assignment all rights to all JHU inventors' interest said valuable Invention; and

WHEREAS, JHU has determined that commercialization of said invention is best served by releasing title back to FRANANO; and

WHEREAS, FRANANO desires to obtain all rights in said invention to pursue commercialization throughout the world;

NOW, THEREFORE, in consideration of the foregoing premises and the following mutual covenants, and other good and valuable consideration, the receipt and sufficiency of which is hereby acknowledged, the parties hereto agree as follows:

**ARTICLE 1**  
**GRANTS**

1.1 JHU hereby assigns all of its intellectual property rights in the Invention to FRANANO, subject to the terms of this agreement and JHU's receipt of any payments as provided for below; the rights retained by the United States government in accordance with P.L. 96-517, as amended by P.L. 98-620; and subject to the approval of the U.S. government under 37 CFR 401.9. This assignment is contingent upon the accuracy of the Report of Invention provided to the Office of Technology Licensing (including, but not

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limited to, information relating to inventorship and sponsorship).

1.2 The assignment of Paragraph 1.1 may be licensed or assigned to third parties, provided that such license or assignment is consistent with the terms of this Agreement.

1.3 JHU shall have the right to review and approve any pertinent provisions of any license agreement for or assignment of the Invention contemplated by FRANANO for the purpose of ensuring that JHU is sufficiently protected under appropriate warranty, representation, indemnification, product liability and use-of-name provisions to be included in such a license agreement or assignment.

1.4 FRANANO hereby grants JHU a paid-up, royalty-free, non-exclusive license to use all intellectual property rights in the Invention for its and The Johns Hopkins Health Systems' nonprofit purposes, including the ability to distribute any biological material covered under Patent Rights for nonprofit academic research use as is customary in the scientific community.

**ARTICLE 2**  
**PATENT MATTERS**

2.1 As applicable, FRANANO agrees to record corrected assignments of Patent Rights at the U.S. Patent and Trademark Office and patent offices within other countries within sixty (60) days of the date of execution of this Agreement.

2.2 FRANANO agrees to reimburse JHU eleven thousand twenty eight dollars (\$11,028) in four (4) equal payments of two thousand seven hundred fifty seven dollars (\$2757). The first payment shall be due upon execution of this Agreement; the second, third and fourth payments shall be due on or before the first, second and third anniversaries respectively.

2.3 FRANANO acknowledges that any future costs regarding patent matters, including but not limited to, costs related to prosecution, maintenance and infringement, are solely the responsibility of FRANANO.

**ARTICLE 3**  
**REPRESENTATIONS**

3.1 Representations by JHU. JHU warrants that it has good and marketable title to its interest in the Invention, with the exception of certain retained rights of the United States government. JHU does not warrant the validity of any patents or that practice under such patents shall be free of infringement. EXCEPT AS EXPRESSLY SET FORTH IN THIS PARAGRAPH, FRANANO AGREES AND SHALL CAUSE EACH LICENSEE,

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SUBLICENSEE AND ASSIGNEE TO AGREE THAT THE PATENT RIGHTS ARE PROVIDED "AS IS", AND THAT JHU MAKES NO REPRESENTATION OR WARRANTY WITH RESPECT TO THE PERFORMANCE OF THE INVENTION INCLUDING ITS SAFETY, EFFECTIVENESS, OR COMMERCIAL VIABILITY. JHU DISCLAIMS ALL WARRANTIES WITH REGARD TO THE INVENTION LICENSED UNDER THIS AGREEMENT, INCLUDING, BUT NOT LIMITED TO, ALL WARRANTIES, EXPRESS OR IMPLIED, OF MERCHANTABILITY AND FITNESS FOR ANY PARTICULAR PURPOSE.





ASSIGNMENT OF PATENT

This Assignment, made and entered into on this 30th day of December, 2002 by and between F. Nicholas Franano, an individual residing in Kansas City, Missouri ("Assignor"), and Proteon Therapeutics, L.L.C., a Missouri Limited Liability Company ("Assignee").

WITNESSETH THAT:

WHEREAS, Assignor is the owner of a certain valuable invention entitled "Local, Transcatheter Delivery of Pretenses to Reopen Obstructed Biological Conduits" (hereinafter referred to as "Invention"), said Invention disclosed and/or claimed in U.S. Provisional Patent Application Serial No. 60,155,938 filed on September 24, 1999, U.S. Patent Application Serial No. 09,669,051 filed on September 24, 2000 and International PCT Application Serial No. PCT;US00/26237 filed on September 24, 2000 (hereinafter referred to as "Patent Rights"); and

WHEREAS, Assignor wishes to transfer ownership in said Invention and Patent Rights to Assignee to facilitate the further development and marketing of said Invention.

NOW THEREFORE, in consideration of the sum of Ten Dollars (\$10.00) and other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, Assignor does hereby assign all of Assignor's right, title, and interest as Inventor in and to the Invention and in and to the Patent Rights, including, but not limited to all patent amendments and/or changes made to finally obtain a Patent and by its signature hereon, Assignee from this date forward agrees to bear all additional charges and costs, if any, associated with the processing of the Patent Application and agrees to save Assignor harmless from any such costs and / or expenses.

IN WITNESS WHEREOF, the parties hereto have executed this Assignment on the day and year first above mentioned.

/s/ F. Nicholas Franano  
F. Nicholas Franano, Assignor

Proteon Therapeutics, L.L.C.

By: /s/ F. Nicholas Franano  
F. Nicholas Franano, Managing Member

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STATE OF MISSOURI )  
 ) ss.  
COUNTY OF JACKSON )

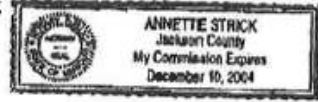
Before me, a Notary Public, in and for said County and State, personally appeared **F. Nicholas Franano**, to me known to be the person described in and who executed the foregoing Assignment and he stated to me that his action thereon was his free act and deed.

Subscribe and sworn to before me this 30<sup>th</sup> day of Dec., 2002.

Annette Strick  
Notary Public

My Commission Expires:

\_\_\_\_\_



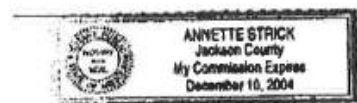
STATE OF MISSOURI )  
 ) ss.  
COUNTY OF JACKSON )

Before me, a Notary Public, in and for said County and State, personally appeared **F. Nicholas Franano**, Managing Member of **Proteon Therapeutics, L.L.C.** to me known to be the person described in and who executed the foregoing Assignment and he stated to me that his action thereon was the free act and deed of said Corporation.

Subscribe and sworn to before me this 30<sup>th</sup> day of Dec., 2002.

Annette Strick  
Notary Public

My Commission Expires:



**PROTEON THERAPEUTICS, INC.  
2006 EQUITY INCENTIVE PLAN**

**STOCK OPTION AGREEMENT**

**(INCENTIVE STOCK OPTION OR NONSTATUTORY STOCK OPTION)**

Pursuant to your Stock Option Grant Notice (“Grant Notice”) and this Stock Option Agreement, **PROTEON THERAPEUTICS, INC.** (the “Company”) has granted you an option under its **2006 EQUITY INCENTIVE PLAN** (the “Plan”) to purchase the number of shares of the Company’s Common Stock indicated in your Grant Notice at the exercise price indicated in your Grant Notice. Defined terms not explicitly defined in this Stock Option Agreement but defined in the Plan shall have the same definitions as in the Plan.

The details of your option are as follows:

1. **VESTING.** Subject to the limitations contained herein, your option will vest as provided in your Grant Notice, provided that vesting will cease upon the termination of your Continuous Service.
2. **NUMBER OF SHARES AND EXERCISE PRICE.** The number of shares of Common Stock subject to your option and your exercise price per share referenced in your Grant Notice may be adjusted from time to time for Capitalization Adjustments.
3. **EXERCISE PRIOR TO VESTING (“EARLY EXERCISE”).** If permitted in your Grant Notice (i.e., the “Exercise Schedule” indicates that “Early Exercise” of your option is permitted) and subject to the provisions of your option, you may elect at any time that is both (i) during the period of your Continuous Service and (ii) during the term of your option, to exercise all or part of your option, including the nonvested portion of your option; *provided, however*, that:
  - (a) a partial exercise of your option shall be deemed to cover first vested shares of Common Stock and then the earliest vesting installment of unvested shares of Common Stock;
  - (b) any shares of Common Stock so purchased from installments that have not vested as of the date of exercise shall be subject to the purchase option in favor of the Company as described in the Company’s form of Early Exercise Stock Purchase Agreement;
  - (c) you shall enter into the Company’s form of Early Exercise Stock Purchase Agreement with a vesting schedule that will result in the same vesting as if no early exercise had occurred; and
  - (d) if your option is an Incentive Stock Option, then, to the extent that the aggregate Fair Market Value (determined at the time of grant) of the shares of Common Stock with respect to which your option plus all other Incentive Stock Options you hold are exercisable for the first time by you during any calendar year (under all plans of the Company and its Affiliates) exceeds one hundred thousand dollars (\$100,000), your option(s) or portions thereof

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that exceed such limit (according to the order in which they were granted) shall be treated as Nonstatutory Stock Options.

4. **METHOD OF PAYMENT.** Payment of the exercise price is due in full upon exercise of all or any part of your option. You may elect to make payment of the exercise price in cash or by check or in any other manner *permitted by your Grant Notice*, which may include one or more of the following:
  - (a) In the Company’s sole discretion at the time your option is exercised and provided that at the time of exercise the Common Stock is publicly traded, pursuant to a program developed under Regulation T as promulgated by the Federal Reserve Board that, prior to the issuance of Common Stock, results in either the receipt of cash (or check) by the Company or the receipt of irrevocable instructions to pay the aggregate exercise price to the Company from the sales proceeds.
  - (b) Provided that at the time of exercise the Common Stock is publicly traded, by delivery of already-owned shares of Common Stock either that you have held for the period required to avoid a charge to the Company’s reported earnings (generally six (6) months) or that you did not acquire, directly or indirectly from the Company, that are owned free and clear of any liens, claims, encumbrances or security interests, and that are valued at Fair Market Value on the date of exercise. “Delivery” for these purposes, in the sole discretion of the Company at the time you exercise your option, shall include delivery to the Company of your attestation of ownership of such shares of Common Stock in a form approved by the Company. Notwithstanding the foregoing, you may not exercise your option by tender to the Company of Common Stock to the extent such tender would violate the provisions of any law, regulation or agreement restricting the redemption of the Company’s stock.
5. **WHOLE SHARES.** You may exercise your option only for whole shares of Common Stock.
6. **SECURITIES LAW COMPLIANCE.** Notwithstanding anything to the contrary contained herein, you may not exercise your option unless the shares of Common Stock issuable upon such exercise are then registered under the Securities Act or, if such shares of Common Stock are not then so registered, the Company has determined that such exercise and issuance would be exempt from the registration requirements of the Securities Act. The exercise of your option also must comply with other applicable laws and regulations governing your option, and you may not exercise your option if the Company determines that such exercise would not be in material compliance with such laws and regulations.
7. **TERM.** You may not exercise your option before the commencement or after the expiration of its term. The term of your option commences on the Date of Grant and expires upon the earliest of the following:
  - (a) three (3) months after the termination of your Continuous Service for any reason other than your Disability or death, provided that if during any part of such three (3) month period your option is not exercisable solely because of the condition set forth in Section 6, your option shall not expire until the earlier of the Expiration Date or until it shall have been

exercisable for an aggregate period of three (3) months after the termination of your Continuous Service;

- (b) twelve (12) months after the termination of your Continuous Service due to your Disability;
- (c) eighteen (18) months after your death if you die either during your Continuous Service or within three (3) months after your Continuous Service terminates;
- (d) the Expiration Date indicated in your Grant Notice; or
- (e) the day before the tenth (10th) anniversary of the Date of Grant.

If your option is an Incentive Stock Option, note that to obtain the federal income tax advantages associated with an Incentive Stock Option, the Code requires that at all times beginning on the date of grant of your option and ending on the day three (3) months before the date of your option's exercise, you must be an employee of the Company or an Affiliate, except in the event of your death or your permanent and total disability, as defined in Section 22(e) of the Code. (The definition of disability in Section 22(e) of the Code is different from the definition of the Disability under the Plan). The Company has provided for extended exercisability of your option under certain circumstances for your benefit but cannot guarantee that your option will necessarily be treated as an Incentive Stock Option if you continue to provide services to the Company or an Affiliate as a Consultant or Director after your employment terminates or if you otherwise exercise your option more than three (3) months after the date your employment with the Company or an Affiliate terminates.

## 8. EXERCISE.

(a) You may exercise the vested portion of your option (and the unvested portion of your option if your Grant Notice so permits) during its term by delivering a Notice of Exercise (in a form designated by the Company) together with the exercise price to the Secretary of the Company, or to such other person as the Company may designate, during regular business hours, together with such additional documents as the Company may then require.

(b) By exercising your option you agree that, as a condition to any exercise of your option, the Company may require you to enter into an arrangement providing for the payment by you to the Company of any tax withholding obligation of the Company arising by reason of (1) the exercise of your option, (2) the lapse of any substantial risk of forfeiture to which the shares of Common Stock are subject at the time of exercise, or (3) the disposition of shares of Common Stock acquired upon such exercise.

(c) If your option is an Incentive Stock Option, by exercising your option you agree that you will notify the Company in writing within fifteen (15) days after the date of any disposition of any of the shares of the Common Stock issued upon exercise of your option that occurs within two (2) years after the date of your option grant or within one (1) year after such shares of Common Stock are transferred upon exercise of your option.

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(d) By exercising your option you agree that you shall not sell, dispose of, transfer, make any short sale of, grant any option for the purchase of, or enter into any hedging or similar transaction with the same economic effect as a sale, any shares of Common Stock or other securities of the Company held by you, for a period of time specified by the managing underwriter(s) (not to exceed one hundred eighty (180) days) following the effective date of a registration statement of the Company filed under the Securities Act (the "Lock Up Period"); *provided, however*, that nothing contained in this section shall prevent the exercise of a repurchase option, if any, in favor of the Company during the Lock Up Period. You further agree to execute and deliver such other agreements as may be reasonably requested by the Company and/or the underwriter(s) that are consistent with the foregoing or that are necessary to give further effect thereto. In order to enforce the foregoing covenant, the Company may impose stop-transfer instructions with respect to your shares of Common Stock until the end of such period. The underwriters of the Company's stock are intended third party beneficiaries of this Section 8(d) and shall have the right, power and authority to enforce the provisions hereof as though they were a party hereto.

9. **TRANSFERABILITY.** Your option is not transferable, except by will or by the laws of descent and distribution, and is exercisable during your life only by you. Notwithstanding the foregoing, by delivering written notice to the Company, in a form satisfactory to the Company, you may designate a third party who, in the event of your death, shall thereafter be entitled to exercise your option.

10. **RIGHT OF FIRST REFUSAL.** Shares of Common Stock that you acquire upon exercise of your option are subject to any right of first refusal that may be described in the Company's bylaws in effect at such time the Company elects to exercise its right; *provided, however*, that if your option is an Incentive Stock Option and the right of first refusal described in the Company's bylaws in effect at the time the Company elects to exercise its right is more beneficial to you than the right of first refusal described in the Company's bylaws on the Date of Grant, then the right of first refusal described in the Company's bylaws on the Date of Grant shall apply. The Company's right of first refusal shall expire on the Listing Date. For purposes of this Agreement, Listing Date shall mean the first date upon which any security of the Company is listed (or approved for listing) upon notice of issuance on a national securities exchange or on the National Market System of the Nasdaq Stock Market (or any successor to that entity).

11. **RIGHT OF REPURCHASE.** To the extent provided in the Company's bylaws in effect at such time the Company elects to exercise its right, the Company shall have the right to repurchase all or any part of the shares of Common Stock you acquire pursuant to the exercise of your option.

12. **OPTION NOT A SERVICE CONTRACT.** Your option is not an employment or service contract, and nothing in your option shall be deemed to create in any way whatsoever any obligation on your part to continue in the employ of the Company or an Affiliate, or of the Company or an Affiliate to continue your employment. In addition, nothing in your option shall obligate the Company or an Affiliate, their respective stockholders, Boards of Directors, Officers or Employees to continue any relationship that you might have as a Director or Consultant for the Company or an Affiliate.

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## 13. WITHHOLDING OBLIGATIONS.

(a) At the time you exercise your option, in whole or in part, or at any time thereafter as requested by the Company, you hereby authorize withholding from payroll and any other amounts payable to you, and otherwise agree to make adequate provision for (including by means of a "cashless exercise" pursuant to a program developed under Regulation T as promulgated by the Federal Reserve Board to the extent permitted by the Company), any sums required to

satisfy the federal, state, local and foreign tax withholding obligations of the Company or an Affiliate, if any, which arise in connection with the exercise of your option.

**(b)** Upon your request and subject to approval by the Company, in its sole discretion, and compliance with any applicable legal conditions or restrictions, the Company may withhold from fully vested shares of Common Stock otherwise issuable to you upon the exercise of your option a number of whole shares of Common Stock having a Fair Market Value, determined by the Company as of the date of exercise, not in excess of the minimum amount of tax required to be withheld by law (or such lower amount as may be necessary to avoid variable award accounting). If the date of determination of any tax withholding obligation is deferred to a date later than the date of exercise of your option, share withholding pursuant to the preceding sentence shall not be permitted unless you make a proper and timely election under Section 83(b) of the Code, covering the aggregate number of shares of Common Stock acquired upon such exercise with respect to which such determination is otherwise deferred, to accelerate the determination of such tax withholding obligation to the date of exercise of your option. Notwithstanding the filing of such election, shares of Common Stock shall be withheld solely from fully vested shares of Common Stock determined as of the date of exercise of your option that are otherwise issuable to you upon such exercise. Any adverse consequences to you arising in connection with such share withholding procedure shall be your sole responsibility.

**(c)** You may not exercise your option unless the tax withholding obligations of the Company and/or any Affiliate are satisfied. Accordingly, you may not be able to exercise your option when desired even though your option is vested, and the Company shall have no obligation to issue a certificate for such shares of Common Stock or release such shares of Common Stock from any escrow provided for herein unless such obligations are satisfied.

**14. NOTICES.** Any notices provided for in your option or the Plan shall be given in writing and shall be deemed effectively given upon receipt during normal business hours by (i) personal delivery, (ii) nationally recognized overnight courier, (iii) by electronic mail or other electronic means, or, (iv) in the case of notices delivered by mail by the Company to you, five (5) days after deposit in the United States mail, postage prepaid, addressed to you at the last address you provided to the Company.

**15. GOVERNING PLAN DOCUMENT.** Your option is subject to all the provisions of the Plan, the provisions of which are hereby made a part of your option, and is further subject to all interpretations, amendments, rules and regulations, which may from time to time be promulgated and adopted pursuant to the Plan. In the event of any conflict between the provisions of your option and those of the Plan, the provisions of the Plan shall control.

## INDEMNIFICATION AGREEMENT

THIS INDEMNIFICATION AGREEMENT (the “**Agreement**”) is; made and entered into as of March 29, 2006 between **PROTEON THERAPEUTICS, INC.**, Delaware corporation (the “**Company**”), and Brendan O’Leary (“**Indemnitee**”),

WITNESSETH THAT:

WHEREAS, highly competent persons have become more reluctant to serve corporations as directors or in other capacities unless they are provided with adequate protection through insurance or adequate indemnification against inordinate risks of claims and actions against them arising out of their service to and activities on behalf of the corporation;

WHEREAS, the Board of Directors of the Company (the “**Board**”) has determined that, in order to attract and retain qualified individuals, the Company will attempt to maintain on an ongoing basis, at its sole expense, liability insurance to protect persons serving the Company and its subsidiaries from certain liabilities. Although the furnishing of such insurance has been a customary and widespread practice among United States-based corporations and other business enterprises, the Company believes that, given current market conditions and trends, such insurance may be available to it in the future only at higher premiums and with more exclusions. At the same time, directors, officers, and other persons in service to corporations or business enterprises are being increasingly subjected to expensive and time-consuming litigation relating to, among other things, matters that traditionally would have been brought only against the Company or business enterprise itself. The Certificate of Incorporation of the Company permits, and the By-laws of the Company require, indemnification of directors of the Company, Indemnitee may also be entitled to indemnification pursuant to the General Corporation Law of the State of Delaware (“**DGCL**”). The By-laws and the DGCL expressly provide that the indemnification provisions set forth therein are not exclusive, and thereby contemplate that contracts may be entered into between the Company and members of the board of directors with respect to indemnification;

WHEREAS, the uncertainties relating to such insurance and to indemnification have increased the difficulty of attracting and retaining such persons;

WHEREAS; the Board has determined that the increased difficulty in attracting and retaining such persons is detrimental to the best interests of the Company’s stockholders and that the Company should act to assure such persons that there will be increased certainty of such protection in the future;

WHEREAS, it is reasonable, prudent and necessary for the Company contractually to obligate itself to indemnify, and to advance expenses on behalf of such persons to the fullest extent permitted by applicable law so that they will serve or continue to serve the Company free from undue concern that they will not be so indemnified;

WHEREAS, this Agreement is a supplement to and in furtherance of the By-laws of the Company and any resolutions adopted pursuant thereto, and shall not be deemed a substitute therefor, nor to diminish or abrogate any rights of Indemnitee thereunder;

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WHEREAS, Indemnitee does not regard the protection available under the Company’s By-laws and insurance as adequate in the present circumstances, and may not be willing to serve as a director without adequate protection, and the Company desires Indemnitee to serve in such capacity. Indemnitee is willing to serve, continue to serve and to take on additional service for or on behalf of the Company on the condition that he be so indemnified; and

NOW, THEREFORE, in consideration of Indemnitee’s agreement to serve as a director after the date hereof, the parties hereto agree as follows:

1. Indemnity of Indemnitee. The Company hereby agrees to hold harmless and indemnify Indemnitee to the fullest extent permitted by law, as such may amended from time to time. In furtherance of the foregoing indemnification, and without limiting the generality thereof:

(a) Proceedings Other Than Proceedings by or in the Right of the Company. Indemnitee shall be entitled to the rights of indemnification provided in this Section 1(a) if, by reason of his Corporate Status (as hereinafter defined), the Indemnitee is, or is threatened to be made, a party to or participant in any Proceeding (as hereinafter defined) other than a Proceeding by or in the right of the Company. Pursuant to this Section 1(a), Indemnitee shall be indemnified against all Expenses (as hereinafter defined), judgments, penalties, fines and amounts paid in settlement actually and reasonably incurred by him, or on his behalf, in connection with such Proceeding or any claim, issue or matter therein, if the Indemnitee acted in good faith and in a manner the Indemnitee reasonably believed to be in or not opposed to the best interests of the Company, and with respect to any criminal Proceeding, had no reasonable cause to believe the Indemnitee’s conduct was unlawful.

(b) Proceedings by or in the Right of the Company. Indemnitee shall be entitled to the rights of indemnification provided in this Section 1(b) if, by reason of his Corporate Status, the Indemnitee is; or is threatened to be made, a party to or participant in any Proceeding brought by or in the right of the Company. Pursuant to this Section 1(b), Indemnitee shall be indemnified against all Expenses actually and reasonably incurred by the Indemnitee, or on the Indemnitee’s behalf, in connection with such Proceeding if the Indemnitee acted in good faith and in a manner the Indemnitee reasonably believed to be in or not opposed to the best interests of the Company; provided, however, if applicable law so provides, no indemnification against such Expenses shall be made in respect of any claim, issue or matter in such Proceeding as to which Indemnitee shall have been adjudged to be liable to the Company unless and to the extent that the Court of Chancery of the State of Delaware shall determine that such indemnification may be made.

(c) Indemnification for Expenses of a Party Who is Wholly or Partly Successful. Notwithstanding any other provision of this Agreement, to the extent that Indemnitee is, by reason of his Corporate Status, a party to and is successful, on the merits or otherwise, in any Proceeding, he shall be indemnified to the maximum extent permitted by law, as such may be amended from time to time, against all Expenses actually and reasonably incurred by him or on his behalf in connection therewith. If Indemnitee is not wholly successful in such Proceeding but is successful, on the merits or otherwise, as to one or more but less than all claims, issues or matters in such Proceeding, the Company shall indemnify Indemnitee against all Expenses actually and reasonably incurred by him or on his behalf in connection with each successfully resolved claim, issue or matter. For purposes of this Section and without

2. Additional Indemnity. In addition to, and without regard to any limitations on, the indemnification provided for in Section 1 of this Agreement, Company shall and hereby does indemnify and hold harmless Indemnitee against all Expenses, judgments, penalties, fines and amounts paid in settlement actually and reasonably incurred by him or on his behalf if, by reason of his Corporate Status, he is, or is threatened to be made a party to or participant in any Proceeding (including a Proceeding by or in the right of the Company), including, without limitation, all liability arising out of the negligence or active or passive wrongdoing of Indemnitee. The only limitation that shall exist upon the Company's obligations pursuant to this Agreement shall be that the Company shall not be obligated to make any payment to Indemnitee that is finally determined (under the procedures, and subject to the presumptions, set forth in Sections 6 and 7 hereof) to be unlawful.

3. Contribution.

(a) Whether or not the indemnification provided in Sections 1 and 2 hereof is available, in respect of any threatened, pending or completed action, suit or proceeding in which the Company is jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding), the Company shall pay, in the first instance, the entire amount of any judgment or settlement of such action, suit or proceeding without requiring Indemnitee to contribute to such payment and the Company hereby waives and relinquishes any right of contribution it may have against Indemnitee. The Company shall not enter into any settlement of any action, suit or proceeding in which the Company is jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding) unless such settlement provides for a full and final release of all claims asserted against Indemnitee.

(b) Without diminishing or impairing the obligations of the Company set forth in the preceding subparagraph, if, for any reason, Indemnitee shall elect or be required to pay all or any portion of any judgment or settlement in any threatened, pending or completed action, suit or proceeding in which the Company is jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding), the Company shall contribute to the amount of expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred and paid or payable by Indemnitee in proportion to the relative benefits received by the Company and all officers, directors or employees of the Company, other than Indemnitee, who are jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding), on the one hand, and Indemnitee, on the other hand, from the transaction from which such action, suit or proceeding arose; provided, however, that the proportion determined on the basis of relative benefit may, to the extent necessary to conform to law, be further adjusted by reference to the relative fault of the Company and all officers, directors or employees of the Company other than Indemnitee who are jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding); on the one hand, and Indemnitee, on the other hand, in connection with the events that resulted in such expenses, judgments, fines or settlement amounts, as well as any other equitable considerations which the Law may require to be considered. The relative fault of the Company and all officers, directors or employees of the Company, other than Indemnitee, who are jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding), on the one hand, and Indemnitee, on the other hand, shall be determined by reference to, among other things, the degree to which their actions were motivated

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by intent to gain personal profit or advantage, the degree to which their liability is primary or secondary and the degree to which their conduct is active or passive.

(c) The Company hereby agrees to fully indemnify and hold Indemnitee harmless from any claims of contribution which may be brought, by officers, directors or employees of the Company, other than Indemnitee, who may be jointly liable with Indemnitee.

(d) To the fullest extent permissible under applicable law, if the indemnification provided for in this Agreement is unavailable to Indemnitee for any reason whatsoever, the Company, in lieu of indemnifying Indemnitee, shall contribute to the amount incurred by Indemnitee, whether for judgments, fines, penalties, excise taxes, amounts paid or to be paid in settlement and/or for Expenses, in connection with any claim relating to an indemnifiable event under this Agreement, in such proportion as is deemed fair and reasonable in light of all of the circumstances of such Proceeding in order to reflect (i) the relative benefits received by the Company and Indemnitee as a result of the events) and/or transaction(s) giving cause to such Proceeding; and/or (ii) the relative fault of the Company (and its directors, officers, employees and agents) and Indemnitee in connection with such event(s) and/or transaction(s).

4. Indemnification for Expenses or a Witness. Notwithstanding any other provision of this Agreement, to the extent that Indemnitee is, by reason of his Corporate Status, a witness in any Proceeding to which Indemnitee is not a party, he shall be indemnified against all Expenses actually and reasonably incurred by him or on his behalf in connection therewith.

5. Advancement of Expenses. Notwithstanding any other provision of this Agreement, the Company shall advance all Expenses incurred by or on behalf of Indemnitee in connection with any Proceeding by reason of Indemnitee's Corporate Status within thirty (30) days after the receipt by the Company of a statement or statements from Indemnitee requesting such advance or advances from time to time, whether prior to or after final disposition of such Proceeding. Such statement or statements shall reasonably evidence the Expenses incurred by Indemnitee and shall include or be preceded or accompanied by an undertaking by or on behalf of Indemnitee to repay any Expenses advanced if it shall ultimately be determined that Indemnitee is not entitled to be indemnified against such Expenses. Any advances and undertakings to repay pursuant to this Section 5 shall be unsecured and interest free.

6. Procedures and Presumptions for Determination of Entitlement to Indemnifications. It the intent of this Agreement to secure for Indemnitee rights of indemnity that are as favorable as may be permitted under the Delaware General Corporation Law and public policy of the State of Delaware. Accordingly, the parties agree that the following procedures and presumptions shall apply in the event of any question as to whether Indemnitee is entitled to indemnification under this Agreement:

(a) To obtain indemnification under this Agreement, Indemnitee shall submit to the Company a written request, including therein or therewith such documentation and information as is reasonably available to Indemnitee and is reasonably necessary to determine Whether and to what extent Indemnitee is entitled to indemnification. The Secretary of the Company shall, promptly upon receipt of such a request for indemnification, advise the Board of Directors in writing that Indemnitee has requested indemnification.

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(b) Upon written request by Indemnitee for indemnification pursuant to the first sentence of Section 6(a) hereof, a determination, if required by applicable law, with respect to Indemnitee's entitlement thereto shall be made in the specific case by one of the following three methods, which shall be at the election of the board: (1) by a majority vote of the disinterested directors, even though less than a quorum, by a committee of disinterested directors designated by a majority vote of the disinterested directors, even though less than a quorum, (2) if there are no disinterested directors or if the disinterested directors so direct, by independent legal counsel in a written opinion to the Board of Directors, a copy of Which shall be delivered to the Indemnitee, or (3) if so directed by the Board of

Directors, by the stockholders of the Company. For purposes hereof, disinterested directors are those members of the board of directors of the Company who are not parties to the action, suit or proceeding in respect of which indemnification is sought by Indemnitee.

(c) If the determination of entitlement to indemnification is to be made by Independent Counsel pursuant to Section 6(b) hereof, the Independent Counsel shall be selected as provided in this Section 6(c). The determination of whether Independent Counsel shall be engaged and the selection of such Independent Counsel shall be made by the Board of Directors. Indemnitee may, within 10 days after such written notice of selection shall have been given, deliver to the Company, as the case may be, a written objection to such selection; provided, however, that such objection may be asserted only on the ground that the Independent Counsel so selected does not meet the requirements of “**Independent Counsel**” as defined in Section 13 of this Agreement, and the objection shall set forth with particularity the factual basis of such assertion. Absent a proper and timely objection, the person so selected shall act as Independent Counsel. If a written objection is made and substantiated, the Independent Counsel selected may not serve as Independent Counsel unless and until such objection is withdrawn or a court has determined that such objection is without merit. If, within 20 days after submission by Indemnitee of a written request for indemnification pursuant to Section 6(a) hereof, no Independent Counsel shall have been selected and not objected to, either the Company or Indemnitee may petition the Court. of Chancery of the State of Delaware or other court of competent jurisdiction for resolution of any objection which shall have been made by the Indemnitee to the Company’s selection of Independent Counsel and/or for the appointment as Independent Counsel of a person Selected by the court or by such other person as the court shall designate, and the person with respect to whom all objections are so resolved or the person so appointed shall act as Independent Counsel under Section 6(b) hereof. The Company shall pay any and all reasonable fees and expenses of Independent Counsel incurred by such Independent Counsel in connection with acting pursuant to Section 6(b) hereof, and the Company shall pay all reasonable fees and s expenses incident to the procedures of this Section 6(c), regardless of the manner in which such Independent Counsel was selected or appointed.

(d) In making a determination with respect to entitlement to indemnification hereunder, the person or persons or entity making such determination shall presume that Indemnitee is entitled to indemnification under this Agreement. Anyone seeking to overcome this presumption shall have the burden of proof and the burden of persuasion by clear and convincing evidence. Neither the failure of the Company (including by its directors or independent legal counsel) to have made a determination prior to the commencement of any action pursuant to this Agreement that indemnification is proper in the circumstances because Indemnitee has met the applicable standard of conduct, nor an actual determination by the Company (including by its directors or independent legal counsel) that Indemnitee has not met

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such applicable standard of conduct, shall be a defense to the action or create a presumption that Indemnitee has not met the applicable standard of conduct.

(e) Indemnitee shall be deemed to have acted in good faith if Indemnitee’s action is based on the records or books of account of the Enterprise hereinafter defined), including financial statements, or on information supplied to Indemnitee by the officers of the Enterprise in the course of their duties, or on the advice of legal counsel for the Enterprise or on information or records given or reports made to the Enterprise by an independent certified public accountant or by an appraiser or other expert selected with reasonable care by the Enterprise. In addition, the knowledge and/or actions, or failure to act, of any director, officer, agent or employee of the Enterprise shall not be imputed to Indemnitee for purposes of determining the right to indemnification under this Agreement. Whether or not the foregoing provisions of this Section 6(e) are satisfied, it shall in any event be presumed that Indemnitee has at all times acted in good faith and in a manner he reasonably believed to be in or not opposed to the best interests of the Company. Anyone seeking to overcome this presumption shall have the burden of proof and the burden of persuasion by clear and convincing evidence.

(f) If the person, persons or entity empowered or selected under Section 6 to determine whether Indemnitee is entitled to indemnification shall not have made a determination within sixty (60) days after receipt by the Company of the request therefor, the requisite determination of entitlement to indemnification shall be deemed to have been made and Indemnitee shall be entitled to such indemnification absent (i) a misstatement by Indemnitee of a material fact, or an omission of a material fact necessary to make Indemnitee’s statement not materially misleading, in connection with their request for indemnification, or (ii) a prohibition of such indemnification under applicable law; provided, however, that such 60-day period may be extended for a reasonable time, not to exceed an additional thirty (30) days, if the person, persons or entity making such determination with respect to entitlement to indemnification in good faith requires such additional time to obtain or evaluate documentation and/or information relating thereto; and provided, further, that the foregoing provisions of this Section 6(f) shall not apply if the determination of entitlement to indemnification is to be made by the stockholders pursuant to Section 6(b) of this Agreement and if (A) within fifteen (15) days after receipt by the Company of the request .for such determination, the Board of Directors or the Disinterested Directors, if appropriate; resolve to submit such determination to the stockholders for their consideration at an annual Meeting thereof to be held within seventy-five (75) days after such receipt and such determination is made thereat, or (B) a special meeting of stockholders is called within fifteen (15) days alter such receipt for the purpose of making such determination, such meeting is held for such purpose within sixty (60) days after having been so called and such determination is made thereat.

(g) Indemnitee shall cooperate with the person, persons or entity making such determination with respect to Indemnitee’s entitlement to indemnification, including, providing to such person, persons or entity upon reasonable advance request any documentation or information which is not privileged or otherwise protected from disclosure and which is reasonably available to Indemnitee and reasonably necessary to such determination. Any Independent Counsel, member of the Board of Directors or stockholder of the Company shall act reasonably and in good faith in making a determination regarding the Indemnitee’s entitlement to indemnification under this Agreement. Any costs or expenses (including attorneys’ fees and disbursements) incurred by Indemnitee in so cooperating with the person, persons or entity making such determination shall be borne by the Company (irrespective of the

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determination as to Indemnitee’s entitlement to indemnification) and the Company hereby indemnifies and agrees to hold Indemnitee harmless therefrom.

(h) The Company acknowledges that a settlement or other disposition short of final judgment may be successful if it permits a party to avoid expense, delay, distraction, disruption and uncertainty. In the event that any action, claim or Proceeding to which Indemnitee is a party is resolved in any manner other than by adverse judgment against Indemnitee (including, without limitation, settlement of such action, claim or proceeding with or without payment of money or other consideration) it shall be presumed that Indemnitee has been successful on the merits or otherwise in such action, suit or proceeding. Anyone seeking to overcome this presumption shall have the burden of proof and the burden of persuasion by clear and convincing evidence.

(i) The termination of any Proceeding or of any claim, issue or matter therein, by judgment, order, settlement or conviction, or upon a plea of nolo contendere or its equivalent, shall not (except as otherwise expressly provided in this Agreement) of itself adversely affect the right of Indemnitee to indemnification or create a presumption that Indemnitee did not act in good faith and in a manner which he reasonably believed to be in or not opposed to the best interests of the Company or, with respect to any criminal Proceeding, that Indemnitee had reasonable cause to believe that his conduct was unlawful.



(a) In the event that (i) determination is made pursuant to Section 6 of this Agreement that Indemnitee is not entitled to indemnification under this Agreement, (ii) advancement of Expenses is not timely made pursuant to Section 5 of this Agreement, (iii) no determination of entitlement to indemnification is made pursuant to Section 6(b) of this Agreement within 90 days after receipt by the Company of the request for indemnification, (iv) payment of indemnification is not made pursuant to this Agreement within ten (10) days after receipt by the Company of a written request therefor or (v) payment of indemnification is not made within ten (10) days after a determination has been made that Indemnitee is entitled to indemnification or such determination is deemed to have been made pursuant to Section 6 of this Agreement, Indemnitee shall be entitled to an adjudication in an appropriate court of the State of Delaware, or in any other court of competent jurisdiction, of Indemnitee's entitlement to such indemnification. Indemnitee shall commence such proceeding seeking an adjudication within 180 days following the date on which Indemnitee first has the right to commence such proceeding pursuant to this Section 7(a). The Company shall not oppose Indemnitee's right to seek any such adjudication.

(b) In the event that a determination shall have been made pursuant to Section 6(b) of this Agreement that Indemnitee is not entitled to indemnification, any judicial proceeding commenced pursuant to this Section 7 shall be conducted in all respects as a de novo trial on the merits, and Indemnitee shall not be prejudiced by reason of the adverse determination under Section 6(b).

(c) If a determination shall have been made pursuant to Section 6(b) of this Agreement that Indemnitee is entitled to indemnification, the Company shall be bound by such determination in any judicial proceeding commenced pursuant to this Section 7, absent (i) a misstatement by Indemnitee of a material fact, or an omission of a material fact necessary to

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make Indemnitee's statement not materially misleading in connection with the application for indemnification, or (ii) a prohibition of such indemnification under applicable law.

(d) In the event that Indemnitee, pursuant to this Section 7, seeks a judicial adjudication of his rights under, or to recover damages for breach of, this Agreement, or to recover under any directors' and officers' liability insurance policies maintained by the Company, the Company shall pay on his behalf, in advance, any and all expenses (of the types described in the definition of Expenses in Section 13 of this Agreement) actually reasonably incurred by him in such judicial adjudication, regardless of whether Indemnitee ultimately is determined to be entitled to such indemnification, advancement of expenses or insurance recovery.

(e) The Company shall be precluded from asserting in any judicial proceeding commenced pursuant to this Section 7 that the procedures and presumptions of this Agreement are not valid, binding and enforceable and shall stipulate in any such court that the Company is bound by all the provisions of this Agreement. The Company shall indemnify Indemnitee against any and all Expenses and, if requested by Indemnitee, shall (within ten (10) days after receipt by the Company of a written request therefore) advance, to the extent not prohibited by law, such expenses to Indemnitee, which are incurred by Indemnitee in connection with any action brought by Indemnitee for indemnification or advance of Expenses from the Company under this Agreement or under any directors and officers' liability insurance policies maintained by the Company, regardless of whether Indemnitee ultimately is determined to be entitled to such indemnification, advancement of Expenses or insurance recovery, as the case may be.

(f) Notwithstanding anything in this Agreement to the contrary, no determination as to entitlement to indemnification under this Agreement shall be required to be made prior to the final disposition of the Proceeding.

8. Non-Exclusivity; Survival of Rights; Insurance; Subrogation.

(a) The rights of indemnification as provided by this Agreement shall not be deemed exclusive or any other rights to which Indemnitee may at any time be entitled under applicable law, the certificate of incorporation of the Company, the Bylaws, any agreement, a vote of stockholders, a resolution of directors or otherwise. No amendment, alteration or repeal of this Agreement or of any provision hereof shall limit or restrict any right of Indemnitee under this Agreement in respect of any action taken or omitted by such Indemnitee in his Corporate Status prior to such amendment, alteration or repeal. To the extent that a change in the Delaware General Corporation Law, whether by statute or judicial decision, permits greater indemnification than would be afforded currently under the Bylaws and this Agreement, it is the intent of the parties hereto that Indemnitee shall enjoy by this Agreement the greater benefits so afforded by such change. No right or remedy herein conferred is intended to be exclusive any other right or remedy, and every other right and remedy shall be cumulative and in addition to every other right and remedy given hereunder or now or hereafter existing at law Or in equity or otherwise. The assertion or employment of any right or remedy hereunder, or otherwise, shall not prevent the concurrent assertion or employment of any other right or remedy.

(b) To the extent that the Company maintains an insurance policy or policies providing liability insurance for directors, officers, employees, or agents or fiduciaries of

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the Company or of any other corporation, partnership, joint venture, trust, employee benefit plan or other enterprise that such person serves at the request of the Company, Indemnitee shall be covered by such policy or policies in accordance with its or their terms to the maximum extent of the coverage available for any director, officer, employee, agent or fiduciary under such policy or policies. If, at the time of the receipt of a notice of a claim pursuant to the terms hereof, the Company has director and officer liability insurance in effect, the Company shall give, prompt notice of the commencement of such proceeding to the insurers in accordance with the procedures set forth in the respective policies. The Company shall thereafter take all necessary or desirable action to cause such insurers to pay, on behalf of the Indemnitee, all amounts payable as a result of such proceeding in accordance with the terms of such policies.

(c) In the event of any payment under this Agreement, the Company shall be subrogated to the extent of such payment to all of the rights of recovery of Indemnitee, who shall execute all papers required and take all action necessary to secure such rights, including execution of such documents as are necessary to enable the Company to bring suit to enforce such rights.

(d) The Company shall not be liable under this Agreement to make any payment of amounts otherwise indemnifiable hereunder. if and to the extent that Indemnitee has otherwise actually received such payment under any insurance policy, contract, agreement or otherwise.

(e) The Company's obligation to indemnify or advance Expenses hereunder to Indemnitee who is or was serving at the request of the Company as a director, officer, employee or agent of any other corporation, partnership, joint venture, trust, employee benefit plan or other enterprise shall be

reduced by any amount Indemnitee has actually received as indemnification or advancement of expenses from such other corporation, partnership, joint venture, trust, employee benefit plan or other enterprise.

9. Exception to Right of Indemnification. Notwithstanding any provision in this Agreement, the Company shall not be obligated under this Agreement to make any indemnity in connection with any claim made against Indemnitee:

(a) for which payment has actually been made to or on behalf of Indemnitee under any insurance policy or other indemnity provision, except with respect to any excess beyond the amount paid under any insurance policy or other indemnity provision; or

(b) for an accounting of profits made from the purchase and sale (or sale and purchase) by Indemnitee of securities of the Company within the meaning of Section 16(b) of the Securities Exchange Act of 1934, as amended, or similar provisions of state statutory law, or common law; or

(c) in connection with any Proceeding (or any part of any Proceeding) initiated by Indemnitee, including any Proceeding (or any part of any Proceeding) initiated by Indemnitee against the Company or its directors, officers, employees or other indemnitees, unless (i) the Board of Directors of the Company authorized the Proceeding (or any part of any Proceeding) prior to its initiation or (ii) the Company provides the indemnification, in its sole discretion, pursuant to the powers vested in the Company under applicable law.

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10. Duration of Agreement. All agreements and obligations of the Company contained herein shall continue during the period Indemnitee is a director of the Company (or is or was serving at the request of the Company as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise) and for a period of five (5) years thereafter, and in addition shall continue thereafter so long as Indemnitee shall be subject to any Proceeding (or any proceeding commenced under Section 7 hereof) by reason of his Corporate Status, whether or not he is acting or serving in any such capacity at the time, any liability or expense is incurred for which indemnification can be provided under this Agreement. This Agreement shall be binding upon and inure to the benefit of and be enforceable by the parties hereto and their respective successors (including any direct or indirect successor by purchase, merger, consolidation or otherwise to all or substantially all of the business or assets of the Company), assigns, spouses, heirs, executors and personal and legal representatives.

11. Security. To the extent requested by Indemnitee and approved by the Board of Directors of the Company, the Company may at any time and from time to time provide security to Indemnitee for the Company's obligations hereunder through an irrevocable bank line of credit, funded trust or other collateral. Any such security, once provided to Indemnitee, may not be revoked or released without the prior written consent of the Indemnitee.

12. Enforcement.

(a) The Company expressly confirms and agrees that it has entered into this Agreement and assumes the obligation imposed on it hereby in order to induce Indemnitee to serve as a director of the Company, and the Company acknowledges that Indemnitee is relying upon this Agreement in serving as a director of the Company.

(b) This Agreement constitutes the entire agreement between the parties hereto with respect to the subject matter hereof and supersedes all prior agreements and understandings, oral, written and implied, between the parties hereto with respect to the subject matter hereof.

13. Definitions. For purposes of this Agreement:

(a) **"Corporate Status"** describes the status of a person who is or was a director, officer, employee, agent or fiduciary of the Company or of any other corporation, partnership, joint venture, trust, employee benefit plan or other enterprise that such person is or was serving at the express written request of the Company.

(b) **"Disinterested Director"** means a director of the Company who is not and was not a party to the Proceeding in respect of which indemnification is sought by Indemnitee.

(c) **"Enterprise"** shall mean the Company and any other corporation, partnership, joint venture, trust, employee benefit plan or other enterprise that Indemnitee is or was serving at the express written request of the Company as a director, officer, employee, agent or fiduciary.

(d) **"Expenses"** shall include all reasonable attorneys' fees, retainers, court costs, transcript costs, fees of experts, witness fees, travel expenses, duplicating costs,

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printing and binding costs, telephone charges, postage, delivery service fees and all other disbursements or expenses of the types customarily incurred in connection with prosecuting, defending, preparing to prosecute or defend, investigating, participating, or being or preparing to be a witness in a Proceeding. Expenses also shall include Expenses incurred in connection with any appeal resulting from any Proceeding, including without limitation the premium, security for, and other costs relating to any cost bond, supersedeas bond, or other appeal bond or its equivalent. Expenses, however, shall not include amounts paid in settlement by Indemnitee or the amount of judgments or fines against Indemnitee.

(e) **"Independent Counsel"** means a law firm, or a member of a law firm, that is experienced in matters of corporation law and neither presently is, nor in the past five years has been, retained to represent: (i) the Company or Indemnitee in any matter material to either such party (other than with respect to matters concerning Indemnitee under this Agreement, or of other indemnitees under similar indemnification, agreements), or (ii) any other party to the Proceeding giving rise to a claim for indemnification hereunder. Notwithstanding the foregoing, the term "Independent Counsel" shall not include any person who, under the applicable standards of professional conduct then prevailing, would have a conflict of interest in representing either the Company or Indemnitee in an action to determine Indemnitee's rights under this Agreement. The Company agrees to pay the reasonable fees of the Independent Counsel referred to above and to fully indemnify such counsel against any and all Expenses, claims, liabilities and damages arising out of or relating to this Agreement or its engagement pursuant hereto.

(f) **"Proceeding"** includes any threatened, pending or completed action, suit, arbitration, alternate dispute resolution mechanism, investigation, inquiry, administrative hearing or any other actual, threatened or completed proceeding, whether brought by or in the right of the Company or otherwise and whether civil, criminal, administrative or investigative, in which Indemnitee was, is or will be involved as a party or otherwise, by reason of the fact

that Indemnitee is or was a director of the Company, by reason of any action taken by him or of any inaction on his part while acting as a director of the Company, or by reason of the fact that he is or was serving at the request of the Company as a director, officer, employee, agent or fiduciary of another corporation, partnership, joint venture, trust or other Enterprise; in each case whether or not he is acting or serving in any such capacity at the time any liability or expense is incurred for which indemnification can be provided under this Agreement; including one pending on or before the date of this Agreement, but excluding one initiated by an Indemnitee pursuant to Section 7 of this Agreement to enforce his rights under this Agreement.

14. Severability. The invalidity of unenforceability of any provision hereof shall in no way affect the validity or enforceability of any other provision. Without limiting the generality of the foregoing, this Agreement is intended to confer upon Indemnitee indemnification rights to the fullest extent permitted by applicable laws. In the event any provision hereof conflicts with any applicable law, such provision shall be deemed modified, consistent with the aforementioned intent, to the extent necessary to resolve such conflict.

15. Modification and Waiver. No supplement, modification, termination or amendment of this Agreement shall be binding unless executed in writing by both of the parties hereto. No waiver of any of the provisions of this Agreement shall be deemed or shall constitute a waiver of any other provisions hereof (whether or not similar) nor shall such waiver constitute a continuing waiver.

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16. Notice By Indemnitee. Indemnitee agrees promptly to notify the Company in writing upon being served with or otherwise receiving any summons, citation, subpoena, complaint, indictment, information or other document relating to any Proceeding or matter which may be subject to indemnification covered hereunder. The failure to so notify the Company shall not relieve the Company of any obligation which it may have to Indemnitee under this Agreement or otherwise unless and only to the extent that such failure or delay materially prejudices the Company.

17. Notices. All notices and other communications given or, made pursuant to this Agreement shall be in writing and shall be deemed effectively given: (a) upon personal delivery to the party to be notified, (b) when sent by confirmed electronic mail or facsimile if sent during normal business hours of the recipient, and if not so confirmed, then on the next business day, (c) five (5) days after having been sent by registered or certified mail, return receipt requested, postage prepaid, or (d) one (1) day after deposit with a nationally recognized overnight courier, specifying next day delivery, with written verification of receipt. All communications shall be sent:

(a) To Indemnitee at the address set forth below Indemnitee's signature hereto.

(b) To the Company at:

4420 Madison Avenue, Suite 180  
Kansas City, MO 64111  
Attention: CEO

or to such other address as may have been furnished to Indemnitee by the Company or to the Company by Indemnitee, as the case may be.

18. Counterparts. This Agreement may be executed in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same Agreement. This Agreement may also be executed and delivered by facsimile signature and in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument.

19. Headings. The headings of the paragraphs of this Agreement are inserted for convenience only and shall not be deemed to constitute part of this Agreement or to affect the construction thereof.

20. Governing Law and Consent to Jurisdiction. This Agreement and the legal relations among the parties shall be governed by, and construed and enforced in accordance with, the laws of the State of Delaware, without regard to its conflict of laws rules. The Company and Indemnitee hereby irrevocably and unconditionally (i) agree that any action or proceeding arising out of or in connection with this Agreement shall be brought only in the Chancery Court of the State of Delaware (the "**Delaware Court**"), and not in any other state or federal court in the United States of America or any court in any other country, (ii) consent to submit to the exclusive jurisdiction of the Delaware Court for purposes of any action or proceeding arising out of or in connection with this Agreement, (iii) waive any objection to the laying of venue of any such action or proceeding in the Delaware Court, and (iv) waive, and agree not to plead or to

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make, any claim that any such action or proceeding brought in the Delaware Court has been brought in an improper or inconvenient forum.

**SIGNATURE PAGE TO FOLLOW**

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IN WITNESS WHEREOF, the parties hereto have executed this Indemnification Agreement on and as of the day and year first above written.

**PROTEON THERAPEUTIC, INC.**

/s/ Nicholas Franano  
F. Nicholas Franano, M.D., M.A.  
Chief Executive Officer

**INDEMNITEE**

/s/ Brendan M. O' Leary  
Brendan O' Leary

Address:  
Prism Venture Partners  
100 Lowder Brooke Drive  
Suite 2500  
Westwood, MA 02090

[SIGNATURE PAGE FOR PROTEON THERAPEUTIC, INC.  
INDEMNIFICATION AGREEMENT]

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IN WITNESS WHEREOF, the parties hereto have executed this Indemnification Agreement on and as of the day and year first above written.

**PROTEON THERAPEUTIC, INC.**

By: \_\_\_\_\_  
Name: \_\_\_\_\_  
Title: \_\_\_\_\_

**INDEMNITEE**

Name: \_\_\_\_\_  
Address: \_\_\_\_\_

[SIGNATURE PAGE FOR PROTEON THERAPEUTIC, INC.  
INDEMNIFICATION AGREEMENT]

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## INDEMNIFICATION AGREEMENT

## INDEMNIFICATION AGREEMENT

THIS INDEMNIFICATION AGREEMENT (the “**Agreement**”) is made and entered into as of June 26, 2007 between **PROTEON THERAPEUTICS, INC.**, a Delaware corporation (the “**Company**”), and Hubert Birmer (“**Indemnitee**”).

WITNESSETH THAT:

WHEREAS, highly competent persons have become more reluctant to serve corporations as directors or in other capacities unless they are provided with adequate protection through insurance or adequate indemnification against inordinate risks of claims and actions against them arising out of their service to and activities on behalf of the corporation;

WHEREAS, the Board of Directors of the Company (the “**Board**”) has determined that, in order to attract and retain qualified individuals, the Company will attempt to maintain on an ongoing basis, at its sole expense, liability insurance to protect persons serving the Company and its subsidiaries from certain liabilities. Although the furnishing of such insurance has been a customary and widespread practice among United States-based corporations and other business enterprises, the Company believes that, given current market conditions and trends, such insurance may be available to it in the future only at higher premiums and with more exclusions. At the same time, directors, officers, and other persons in service to corporations or business enterprises are being increasingly subjected to expensive and time-consuming litigation relating to, among other things, matters that traditionally would have been brought only against the Company or business enterprise itself. The Certificate of Incorporation of the Company permits, and the By-laws of the Company require, indemnification of directors of the Company. Indemnitee may also be entitled to indemnification pursuant to the General Corporation Law of the State of Delaware (“**DGCL**”). The By-laws and the DGCL expressly provide that the indemnification provisions set forth therein are not exclusive, and thereby contemplate that contracts may be entered into between the Company and members of the board of directors with respect to indemnification;

WHEREAS, the uncertainties relating to such insurance and to indemnification have increased the difficulty of attracting and retaining such persons;

WHEREAS, the Board has determined that the increased difficulty in attracting and retaining such persons is detrimental to the best interests of the Company’s stockholders and that the Company should act to assure such persons that there will be increased certainty of such protection in the future;

WHEREAS, it is reasonable, prudent and necessary for the Company contractually to obligate itself to indemnify, and to advance expenses on behalf of, such persons to the fullest extent permitted by applicable law so that they will serve or continue to serve the Company free from undue concern that they will not be so indemnified;

WHEREAS, this Agreement is a supplement to and in furtherance of the By-laws of the Company and any resolutions adopted pursuant thereto, and shall not be deemed a substitute therefor, nor to diminish or abrogate any rights of Indemnitee thereunder;

WHEREAS, Indemnitee does not regard the protection available under the Company’s By-laws and insurance as adequate in the present circumstances, and may not be willing to serve as a director without adequate protection, and the Company desires Indemnitee to serve in such capacity. Indemnitee is willing to serve, continue to serve and to take on additional service for or on behalf of the Company on the condition that he be so indemnified; and

NOW, THEREFORE, in consideration of Indemnitee’s agreement to serve as a director after the date hereof, the parties hereto agree as follows:

1. Indemnity of Indemnitee. The Company hereby agrees to hold harmless and indemnify Indemnitee to the fullest extent permitted by law, as such may be amended from time to time. In furtherance of the foregoing indemnification, and without limiting the generality thereof:

(a) Proceedings Other Than Proceedings by or in the Right of the Company. Indemnitee shall be entitled to the rights of indemnification provided in this Section 1(a) if, by reason of his Corporate Status (as hereinafter defined), the Indemnitee is, or is threatened to be made, a party to or participant in any Proceeding (as hereinafter defined) other than a Proceeding by or in the right of the Company. Pursuant to this Section 1(a), Indemnitee shall be indemnified against all Expenses (as hereinafter defined), judgments, penalties, fines and amounts paid in settlement actually and reasonably incurred by him, or on his behalf, in connection with such Proceeding or any claim, issue or matter therein, if the Indemnitee acted in good faith and in a manner the Indemnitee reasonably believed to be in or not opposed to the best interests of the Company, and with respect to any criminal Proceeding, had no reasonable cause to believe the Indemnitee’s conduct was unlawful.

(b) Proceedings by or in the Right of the Company. Indemnitee shall be entitled to the rights of indemnification provided in this Section 1(b) if, by reason of his Corporate Status, the Indemnitee is, or is threatened to be made, a party to or participant in any Proceeding brought by or in the right of the Company. Pursuant to this Section 1(b), Indemnitee shall be indemnified against all Expenses actually and reasonably incurred by the Indemnitee, or on the Indemnitee’s behalf, in connection with such Proceeding if the Indemnitee acted in good faith and in a manner the Indemnitee reasonably believed to be in or not opposed to the best interests of the Company; provided, however, if applicable law so provides, no indemnification against such Expenses shall be made in respect of any claim, issue or matter in such Proceeding as to which Indemnitee shall have been adjudged to be liable to the Company unless and to the extent that the Court of Chancery of the State of Delaware shall determine that such indemnification may be made.

(c) Indemnification for Expenses of a Party Who is Wholly or Partly Successful. Notwithstanding any other provision of this Agreement, to the extent that Indemnitee is, by reason of his Corporate Status, a party to and is successful, on the merits or otherwise, in any Proceeding, he shall be indemnified to the maximum extent permitted by law, as such may be amended from time to time, against all Expenses actually and reasonably incurred by him or on his behalf in connection therewith. If Indemnitee is not wholly successful in such Proceeding but is successful, on the merits or otherwise, as to one or more but less than all claims, issues or matters in such Proceeding, the Company shall indemnify Indemnitee against all Expenses actually and reasonably incurred by him or on his behalf in connection with each successfully resolved claim, issue or matter. For purposes of this Section and without

limitation, the termination of any claim, issue or matter in such a Proceeding by dismissal, with or without prejudice, shall be deemed to be a successful result as to such claim, issue or matter.

2. Additional Indemnity. In addition to, and without regard to any limitations on, the indemnification provided for in Section 1 of this Agreement, the Company shall and hereby does indemnify and hold harmless Indemnitee against all Expenses, judgments, penalties, fines and amounts paid in settlement actually and reasonably incurred by him or on his behalf if, by reason of his Corporate Status, he is, or is threatened to be made, a party to or participant in any Proceeding (including a Proceeding by or in the right of the Company), including, without limitation, all liability arising out of the negligence or active or passive wrongdoing of Indemnitee. The only limitation that shall exist upon the Company's obligations pursuant to this Agreement shall be that the Company shall not be obligated to make any payment to Indemnitee that is finally determined (under the procedures, and subject to the presumptions, set forth in Sections 6 and 7 hereof) to be unlawful.

3. Contribution.

(a) Whether or not the indemnification provided in Sections 1 and 2 hereof is available, in respect of any threatened, pending or completed action, suit or proceeding in which the Company is jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding), the Company shall pay, in the first instance, the entire amount of any judgment or settlement of such action, suit or proceeding without requiring Indemnitee to contribute to such payment and the Company hereby waives and relinquishes any right of contribution it may have against Indemnitee. The Company shall not enter into any settlement of any action, suit or proceeding in which the Company is jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding) unless such settlement provides for a full and final release of all claims asserted against Indemnitee.

(b) Without diminishing or impairing the obligations of the Company set forth in the preceding subparagraph, if, for any reason, Indemnitee shall elect or be required to pay all or any portion of any judgment or settlement in any threatened, pending or completed action, suit or proceeding in which the Company is jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding), the Company shall contribute to the amount of expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred and paid or payable by Indemnitee in proportion to the relative benefits received by the Company and all officers, directors or employees of the Company, other than Indemnitee, who are jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding), on the one hand, and Indemnitee, on the other hand, from the transaction from which such action, suit or proceeding arose; provided, however, that the proportion determined on the basis of relative benefit may, to the extent necessary to conform to law, be further adjusted by reference to the relative fault of the Company and all officers, directors or employees of the Company other than Indemnitee who are jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding), on the one hand, and Indemnitee, on the other hand, in connection with the events that resulted in such expenses, judgments, fines or settlement amounts, as well as any other equitable considerations which the Law may require to be considered. The relative fault of the Company and all officers, directors or employees of the Company, other than Indemnitee, who are jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding), on the one hand, and Indemnitee, on the other hand, shall be determined by reference to, among other things, the degree to which their actions were motivated

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by intent to gain personal profit or advantage, the degree to which their liability is primary or secondary and the degree to which their conduct is active or passive.

(c) The Company hereby agrees to fully indemnify and hold Indemnitee harmless from any claims of contribution which may be brought by officers, directors or employees of the Company, other than Indemnitee, who may be jointly liable with Indemnitee.

(d) To the fullest extent permissible under applicable law, if the indemnification provided for in this Agreement is unavailable to Indemnitee for any reason whatsoever, the Company, in lieu of indemnifying Indemnitee, shall contribute to the amount incurred by Indemnitee, whether for judgments, fines, penalties, excise taxes, amounts paid or to be paid in settlement and/or for Expenses, in connection with any claim relating to an indemnifiable event under this Agreement, in such proportion as is deemed fair and reasonable in light of all of the circumstances of such Proceeding in order to reflect (i) the relative benefits received by the Company and Indemnitee as a result of the event(s) and/or transaction(s) giving cause to such Proceeding; and/or (ii) the relative fault of the Company (and its directors, officers, employees and agents) and Indemnitee in connection with such event(s) and/or transaction(s).

4. Indemnification for Expenses of a Witness. Notwithstanding any other provision of this Agreement, to the extent that Indemnitee is, by reason of his Corporate Status, a witness in any Proceeding to which Indemnitee is not a party, he shall be indemnified against all Expenses actually and reasonably incurred by him or on his behalf in connection therewith.

5. Advancement of Expenses. Notwithstanding any other provision of this Agreement, the Company shall advance all Expenses incurred by or on behalf of Indemnitee in connection with any Proceeding by reason of Indemnitee's Corporate Status within thirty (30) days after the receipt by the Company of a statement or statements from Indemnitee requesting such advance or advances from time to time, whether prior to or after final disposition of such Proceeding. Such statement or statements shall reasonably evidence the Expenses incurred by Indemnitee and shall include or be preceded or accompanied by an undertaking by or on behalf of Indemnitee to repay any Expenses advanced if it shall ultimately be determined that Indemnitee is not entitled to be indemnified against such Expenses. Any advances and undertakings to repay pursuant to this Section 5 shall be unsecured and interest free.

6. Procedures and Presumptions for Determination of Entitlement to Indemnification. It is the intent of this Agreement to secure for Indemnitee rights of indemnity that are as favorable as may be permitted under the Delaware General Corporation Law and public policy of the State of Delaware. Accordingly, the parties agree that the following procedures and presumptions shall apply in the event of any question as to whether Indemnitee is entitled to indemnification under this Agreement:

(a) To obtain indemnification under this Agreement, Indemnitee shall submit to the Company a written request, including therein or therewith such documentation and information as is reasonably available to Indemnitee and is reasonably necessary to determine whether and to what extent Indemnitee is entitled to indemnification. The Secretary of the Company shall, promptly upon receipt of such a request for indemnification, advise the Board of Directors in writing that Indemnitee has requested indemnification.

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(b) Upon written request by Indemnitee for indemnification pursuant to the first sentence of Section 6(a) hereof, a determination, if required by applicable law, with respect to Indemnitee's entitlement thereto shall be made in the specific case by one of the following three methods, which shall be at the election of the board: (1) by a majority vote of the disinterested directors, even though less than a quorum, by a committee of disinterested directors designated by a majority vote of the disinterested directors, even though less than a quorum, (2) if there are no disinterested directors or if the disinterested directors so direct, by independent legal counsel in a written opinion to the Board of Directors, a copy of which shall be delivered to the Indemnitee, or (3) if so directed by the Board of Directors, by the stockholders of the Company. For purposes hereof; disinterested directors are those members of the board of directors of the Company who are not parties to the action, suit or proceeding in respect of which indemnification is sought by Indemnitee.

(c) If the determination of entitlement to indemnification is to be made by Independent Counsel pursuant to Section 6(b) hereof, the Independent Counsel shall be selected as provided in this Section 6(c). The determination of whether Independent Counsel shall be engaged and the selection of such Independent Counsel shall be made by the Board of Directors. Indemnitee may, within 10 days after such written notice of selection shall have been given, deliver to the Company, as the case may be, a written objection to such selection; provided, however, that such objection may be asserted only on the ground that the Independent Counsel so selected does not meet the requirements of "**Independent Counsel**" as defined in Section 13 of this Agreement, and the objection shall set forth with particularity the factual basis of such assertion. Absent a proper and timely objection, the person so selected shall act as Independent Counsel. If a written objection is made and substantiated, the Independent Counsel selected may not serve as Independent Counsel unless and until such objection is withdrawn or a court has determined that such objection is without merit. If, within 20 days after submission by Indemnitee of a written request for indemnification pursuant to Section 6(a) hereof, no Independent Counsel shall have been selected and not objected to, either the Company or Indemnitee may petition the Court of Chancery of the State of Delaware or other court of competent jurisdiction for resolution of any objection which shall have been made by the Indemnitee to the Company's selection of Independent Counsel and/or for the appointment as Independent Counsel of a person selected by the court or by such other person as the court shall designate, and the person with respect to whom all objections are so resolved or the person so appointed shall act as Independent Counsel under Section 6(b) hereof. The Company shall pay any and all reasonable fees and expenses of Independent Counsel incurred by such Independent Counsel in connection with acting pursuant to Section 6(b) hereof, and the Company shall pay all reasonable fees and expenses incident to the procedures of this Section 6(c), regardless of the manner in which such Independent Counsel was selected or appointed.

(d) In making a determination with respect to entitlement to indemnification hereunder, the person or persons or entity making such determination shall presume that Indemnitee is entitled to indemnification under this Agreement. Anyone seeking to overcome this presumption shall have the burden of proof and the burden of persuasion by clear and convincing evidence. Neither the failure of the Company (including by its directors or independent legal counsel) to have made a determination prior to the commencement of any action pursuant to this Agreement that indemnification is proper in the circumstances because Indemnitee has met the applicable standard of conduct, nor an actual determination by the Company (including by its directors or independent legal counsel) that Indemnitee has not met

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such applicable standard of conduct, shall be a defense to the action or create a presumption that Indemnitee has not met the applicable standard of conduct.

(e) Indemnitee shall be deemed to have acted in good faith if Indemnitee's action is based on the records or books of account of the Enterprise (as hereinafter defined), including financial statements, or on information supplied to Indemnitee by the officers of the Enterprise in the course of their duties, or on the advice of legal counsel for the Enterprise or on information or records given or reports made to the Enterprise by an independent certified public accountant or by an appraiser or other expert selected with reasonable care by the Enterprise. In addition, the knowledge and/or actions, or failure to act, of any director, officer, agent or employee of the Enterprise shall not be imputed to Indemnitee for purposes of determining the right to indemnification under this Agreement. Whether or not the foregoing provisions of this Section 6(e) are satisfied, it shall in any event be presumed that Indemnitee has at all times acted in good faith and in a manner he reasonably believed to be in or not opposed to the best interests of the Company. Anyone seeking to overcome this presumption shall have the burden of proof and the burden of persuasion by clear and convincing evidence.

(f) If the person, persons or entity empowered or selected under Section 6 to determine whether Indemnitee is entitled to indemnification shall not have made a determination within sixty (60) days after receipt by the Company of the request therefor, the requisite determination of entitlement to indemnification shall be deemed to have been made and Indemnitee shall be entitled to such indemnification absent (i) a misstatement by Indemnitee of a material fact, or an omission of a material fact necessary to make Indemnitee's statement not materially misleading, in connection with the request for indemnification, or (ii) a prohibition of such indemnification under applicable law; provided, however, that such 60-day period may be extended for a reasonable time, not to exceed an additional thirty (30) days, if the person, persons or entity making such determination with respect to entitlement to indemnification in good faith requires such additional time to obtain or evaluate documentation and/or information relating thereto; and provided, further, that the foregoing provisions of this Section 6(f) shall not apply if the determination of entitlement to indemnification is to be made by the stockholders pursuant to Section 6(b) of this Agreement and if (A) within fifteen (15) days after receipt by the Company of the request for such determination, the Board of Directors or the Disinterested Directors, if appropriate, resolve to submit such determination to the stockholders for their consideration at an annual meeting thereof to be held within seventy-five (75) days after such receipt and such determination is made thereat, or (B) a special meeting of stockholders is called within fifteen (15) days after such receipt for the purpose of making such determination, such meeting is held for such purpose within sixty (60) days after having been so called and such determination is made thereat.

(g) Indemnitee shall cooperate with the person, persons or entity making such determination with respect to Indemnitee's entitlement to indemnification, including providing to such person, persons or entity upon reasonable advance request any documentation or information which is not privileged or otherwise protected from disclosure and which is reasonably available to Indemnitee and reasonably necessary to such determination. Any Independent Counsel, member of the Board of Directors or stockholder of the Company shall act reasonably and in good faith in making a determination regarding the Indemnitee's entitlement to indemnification under this Agreement. Any costs or expenses (including attorneys' fees and disbursements) incurred by Indemnitee in so cooperating with the person, persons or entity making such determination shall be borne by the Company (irrespective of the

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determination as to Indemnitee's entitlement to indemnification) and the Company hereby indemnifies and agrees to hold Indemnitee harmless therefrom.

(h) The Company acknowledges that a settlement or other disposition short of final judgment may be successful if it permits a party to avoid expense, delay, distraction, disruption and uncertainty. In the event that any action, claim or proceeding to which Indemnitee is a party is resolved in any manner other than by adverse judgment against Indemnitee (including, without limitation, settlement of such action, claim or proceeding with or without payment of money or other consideration) it shall be presumed that Indemnitee has been successful on the merits or otherwise in such action, suit or proceeding. Anyone seeking to overcome this presumption shall have the burden of proof and the burden of persuasion by clear and convincing evidence.

(i) The termination of any Proceeding or of any claim, issue or matter therein, by judgment, order, settlement or conviction, or upon a plea of nolo contendere or its equivalent, shall not (except as otherwise expressly provided in this Agreement) of itself adversely affect the right of Indemnitee to indemnification or create a presumption that Indemnitee did not act in good faith and in a manner which he reasonably believed to be in or not opposed to the best interests of the Company or, with respect to any criminal Proceeding, that Indemnitee had reasonable cause to believe that his conduct was unlawful.

7. Remedies of Indemnitee.

(a) In the event that (i) a determination is made pursuant to Section 6 of this Agreement that Indemnitee is not entitled to indemnification under this Agreement, (ii) advancement of Expenses is not timely made pursuant to Section 5 of this Agreement, (iii) no determination of entitlement to indemnification is made pursuant to Section 6(b) of this Agreement within 90 days after receipt by the Company of the request for indemnification, (iv) payment of indemnification is not made pursuant to this Agreement within ten (10) days after receipt by the Company of a written request therefor or (v) payment of indemnification is not made within ten (10) days after a determination has been made that Indemnitee is entitled to indemnification or such determination is deemed to have been made pursuant to Section 6 of this Agreement, Indemnitee shall be entitled to an adjudication in an appropriate court of the State of Delaware, or in any other court of competent jurisdiction, of Indemnitee's entitlement to such indemnification. Indemnitee shall commence such proceeding seeking an adjudication within 180 days following the date on which Indemnitee first has the right to commence such proceeding pursuant to this Section 7(a). The Company shall not oppose Indemnitee's right to seek any such adjudication.

(b) In the event that a determination shall have been made pursuant to Section 6(b) of this Agreement that Indemnitee is not entitled to indemnification, any judicial proceeding commenced pursuant to this Section 7 shall be conducted in all respects as a de novo trial on the merits, and Indemnitee shall not be prejudiced by reason of the adverse determination under Section 6(b).

(c) If a determination shall have been made pursuant to Section 6(b) of this Agreement that Indemnitee is entitled to indemnification, the Company shall be bound by such determination in any judicial proceeding commenced pursuant to this Section 7, absent (i) a misstatement by Indemnitee of a material fact, or an omission of a material fact necessary to

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make Indemnitee's statement not materially misleading in connection with the application for indemnification, or (ii) a prohibition of such indemnification under applicable law.

(d) In the event that Indemnitee, pursuant to this Section 7, seeks a judicial adjudication of his rights under, or to recover damages for breach of, this Agreement, or to recover under any directors' and officers' liability insurance policies maintained by the Company, the Company shall pay on his behalf, in advance, any and all expenses (of the types described in the definition of Expenses in Section 13 of this Agreement) actually and reasonably incurred by him in such judicial adjudication, regardless of whether Indemnitee ultimately is determined to be entitled to such indemnification, advancement of expenses or insurance recovery.

(e) The Company shall be precluded from asserting in any judicial proceeding commenced pursuant to this Section 7 that the procedures and presumptions of this Agreement are not valid, binding and enforceable and shall stipulate in any such court that the Company is bound by all the provisions of this Agreement. The Company shall indemnify Indemnitee against any and all Expenses and, if requested by Indemnitee, shall (within ten (10) days after receipt by the Company of a written request therefore) advance, to the extent not prohibited by law, such expenses to Indemnitee, which are incurred by Indemnitee in connection with any action brought by Indemnitee for indemnification or advance of Expenses from the Company under this Agreement or under any directors' and officers' liability insurance policies maintained by the Company, regardless of whether Indemnitee ultimately is determined to be entitled to such indemnification, advancement of Expenses or insurance recovery, as the case may be.

(f) Notwithstanding anything in this Agreement to the contrary, no determination as to entitlement to indemnification under this Agreement shall be required to be made prior to the final disposition of the Proceeding.

8. Non-Exclusivity; Survival of Rights; Insurance; Subrogation.

(a) The rights of indemnification as provided by this Agreement shall not be deemed exclusive of any other rights to which Indemnitee may at any time be entitled under applicable law, the certificate of incorporation of the Company, the Bylaws, any agreement, a vote of stockholders, a resolution of directors or otherwise. No amendment, alteration or repeal of this Agreement or of any provision hereof shall limit or restrict any right of Indemnitee under this Agreement in respect of any action taken or omitted by such Indemnitee in his Corporate Status prior to such amendment, alteration or repeal. To the extent that a change in the Delaware General Corporation Law, whether by statute or judicial decision, permits greater indemnification than would be afforded currently under the Bylaws and this Agreement, it is the intent of the parties hereto that Indemnitee shall enjoy by this Agreement the greater benefits so afforded by such change. No right or remedy herein conferred is intended to be exclusive of any other right or remedy, and every other right and remedy shall be cumulative and in addition to every other right and remedy given hereunder or now or hereafter existing at law or in equity or otherwise. The assertion or employment of any right or remedy hereunder, or otherwise, shall not prevent the concurrent assertion or employment of any other right or remedy.

(b) To the extent that the Company maintains an insurance policy or policies providing liability insurance for directors, officers, employees, or agents or fiduciaries of

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the Company or of any other corporation, partnership, joint venture, trust, employee benefit plan or other enterprise that such person serves at the request of the Company, Indemnitee shall be covered by such policy or policies in accordance with its or their terms to the maximum extent of the coverage available for any director, officer, employee, agent or fiduciary under such policy or policies. If, at the time of the receipt of a notice of a claim pursuant to the terms hereof, the Company has director and officer liability insurance in effect, the Company shall give prompt notice of the commencement of such proceeding to the insurers in accordance with the procedures set forth in the respective policies. The Company shall thereafter take all necessary or desirable action to cause such insurers to pay, on behalf of the Indemnitee, all amounts payable as a result of such proceeding in accordance with the terms of such policies.

(c) In the event of any payment under this Agreement, the Company shall be subrogated to the extent of such payment to all of the rights of recovery of Indemnitee, who shall execute all papers required and take all action necessary to secure such rights, including execution of such documents as are necessary to enable the Company to bring suit to enforce such rights.



(d) The Company shall not be liable under this Agreement to make any payment of amounts otherwise indemnifiable hereunder if and to the extent that Indemnitee has otherwise actually received such payment under any insurance policy, contract, agreement or otherwise.

(e) The Company's obligation to indemnify or advance Expenses hereunder to Indemnitee who is or was serving at the request of the Company as a director, officer, employee or agent of any other corporation, partnership, joint venture, trust, employee benefit plan or other enterprise shall be reduced by any amount Indemnitee has actually received as indemnification or advancement of expenses from such other corporation, partnership, joint venture, trust, employee benefit plan or other enterprise.

9. **Exception to Right of Indemnification.** Notwithstanding any provision in this Agreement, the Company shall not be obligated under this Agreement to make any indemnity in connection with any claim made against Indemnitee:

(a) for which payment has actually been made to or on behalf of Indemnitee under any insurance policy or other indemnity provision, except with respect to any excess beyond the amount paid under any insurance policy or other indemnity provision; or

(b) for an accounting of profits made from the purchase and sale (or sale and purchase) by Indemnitee of securities of the Company within the meaning of Section 16(b) of the Securities Exchange Act of 1934, as amended, or similar provisions of state statutory law or common law; or

(c) in connection with any Proceeding (or any part of any Proceeding) initiated by Indemnitee, including any Proceeding (or any part of any Proceeding) initiated by Indemnitee against the Company or its directors, officers, employees or other indemnitees, unless (i) the Board of Directors of the Company authorized the Proceeding (or any part of any Proceeding) prior to its initiation or (ii) the Company provides the indemnification, in its sole discretion, pursuant to the powers vested in the Company under applicable law.

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10. **Duration of Agreement.** All agreements and obligations of the Company contained herein shall continue during the period Indemnitee is a director of the Company (or is or was serving at the request of the Company as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise) and for a period of five (5) years thereafter, and in addition shall continue thereafter so long as Indemnitee shall be subject to any Proceeding (or any proceeding commenced under Section 7 hereof) by reason of his Corporate Status, whether or not he is acting or serving in any such capacity at the time any liability or expense is incurred for which indemnification can be provided under this Agreement. This Agreement shall be binding upon and inure to the benefit of and be enforceable by the parties hereto and their respective successors (including any direct or indirect successor by purchase, merger, consolidation or otherwise to all or substantially all of the business or assets of the Company), assigns, spouses, heirs, executors and personal and legal representatives.

11. **Security.** To the extent requested by Indemnitee and approved by the Board of Directors of the Company, the Company may at any time and from time to time provide security to Indemnitee for the Company's obligations hereunder through an irrevocable bank line of credit, funded trust or other collateral. Any such security, once provided to Indemnitee, may not be revoked or released without the prior written consent of the Indemnitee.

12. **Enforcement.**

(a) The Company expressly confirms and agrees that it has entered into this Agreement and assumes the obligations imposed on it hereby in order to induce Indemnitee to serve as a director of the Company, and the Company acknowledges that Indemnitee is relying upon this Agreement in serving as a director of the Company.

(b) This Agreement constitutes the entire agreement between the parties hereto with respect to the subject matter hereof and supersedes all prior agreements and understandings, oral, written and implied, between the parties hereto with respect to the subject matter hereof.

13. **Definitions.** For purposes of this Agreement:

(a) "**Corporate Status**" describes the status of a person who is or was a director, officer, employee, agent or fiduciary of the Company or of any other corporation, partnership, joint venture, trust, employee benefit plan or other enterprise that such person is or was serving at the express written request of the Company.

(b) "**Disinterested Director**" means a director of the Company who is not and was not a party to the Proceeding in respect of which indemnification is sought by Indemnitee.

(c) "**Enterprise**" shall mean the Company and any other corporation, partnership, joint venture, trust, employee benefit plan or other enterprise that Indemnitee is or was serving at the express written request of the Company as a director, officer, employee, agent or fiduciary.

(d) "**Expenses**" shall include all reasonable attorneys' fees, retainers, court costs, transcript costs, fees of experts, witness fees, travel expenses, duplicating costs,

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printing and binding costs, telephone charges, postage, delivery service fees and all other disbursements or expenses of the types customarily incurred in connection with prosecuting, defending, preparing to prosecute or defend, investigating, participating, or being or preparing to be a witness in a Proceeding. Expenses also shall include Expenses incurred in connection with any appeal resulting from any Proceeding, including without limitation the premium, security for, and other costs relating to any cost bond, supersedeas bond, or other appeal bond or its equivalent. Expenses, however, shall not include amounts paid in settlement by Indemnitee or the amount of judgments or fines against Indemnitee.

(e) "**Independent Counsel**" means a law firm, or a member of a law firm, that is experienced in matters of corporation law and neither presently is, nor in the past five years has been, retained to represent: (i) the Company or Indemnitee in any matter material to either such party (other than with respect to matters concerning Indemnitee under this Agreement, or of other indemnitees under similar indemnification agreements), or (ii) any other party to the Proceeding giving rise to a claim for indemnification hereunder. Notwithstanding the foregoing, the term "Independent Counsel" shall not include any person who, under the applicable standards of professional conduct then prevailing, would have a conflict of interest in representing either the Company or Indemnitee in an action to determine Indemnitee's rights under this Agreement. The Company agrees to pay the reasonable fees of the Independent Counsel referred to above and to fully indemnify such counsel against any and all Expenses, claims, liabilities and damages arising out of or relating to this Agreement or its engagement pursuant hereto.

(f) **“Proceeding”** includes any threatened, pending or completed action, suit, arbitration, alternate dispute resolution mechanism, investigation, inquiry, administrative hearing or any other actual, threatened or completed proceeding, whether brought by or in the right of the Company or otherwise and whether civil, criminal, administrative or investigative, in which Indemnitee was, is or will be involved as a party or otherwise, by reason of the fact that Indemnitee is or was a director of the Company, by reason of any action taken by him or of any inaction on his part while acting as a director of the Company, or by reason of the fact that he is or was serving at the request of the Company as a director, officer, employee, agent or fiduciary of another corporation, partnership, joint venture, trust or other Enterprise; in each case whether or not he is acting or serving in any such capacity at the time any liability or expense is incurred for which indemnification can be provided under this Agreement; including one pending on or before the date of this Agreement, but excluding one initiated by an Indemnitee pursuant to Section 7 of this Agreement to enforce his rights under this Agreement.

14. **Severability.** The invalidity of unenforceability of any provision hereof shall in no way affect the validity or enforceability of any other provision. Without limiting the generality of the foregoing, this Agreement is intended to confer upon Indemnitee indemnification rights to the fullest extent permitted by applicable laws. In the event any provision hereof conflicts with any applicable law, such provision shall be deemed modified, consistent with the aforementioned intent, to the extent necessary to resolve such conflict.

15. **Modification and Waiver.** No supplement, modification, termination or amendment of this Agreement shall be binding unless executed in writing by both of the parties hereto. No waiver of any of the provisions of this Agreement shall be deemed or shall constitute a waiver of any other provisions hereof (whether or not similar) nor shall such waiver constitute a continuing waiver.

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16. **Notice By Indemnitee.** Indemnitee agrees promptly to notify the Company in writing upon being served with or otherwise receiving any summons, citation, subpoena, complaint, indictment, information or other document relating to any Proceeding or matter which may be subject to indemnification covered hereunder. The failure to so notify the Company shall not relieve the Company of any obligation which it may have to Indemnitee under this Agreement or otherwise unless and only to the extent that such failure or delay materially prejudices the Company.

17. **Notices.** All notices and other communications given or made pursuant to this Agreement shall be in writing and shall be deemed effectively given: (a) upon personal delivery to the party to be notified, (b) when sent by confirmed electronic mail or facsimile if sent during normal business hours of the recipient, and if not so confirmed, then on the next business day, (c) five (5) days after having been sent by registered or certified mail, return receipt requested, postage prepaid, or (d) one (1) day after deposit with a nationally recognized overnight courier, specifying next day delivery, with written verification of receipt. All communications shall be sent:

(a) To Indemnitee at the address set forth below Indemnitee’s signature hereto.

(b) To the Company at:

200 West Street  
Waltham, MA 02451  
Attention: CEO

or to such other address as may have been furnished to Indemnitee by the Company or to the Company by Indemnitee, as the case may be.

18. **Counterparts.** This Agreement may be executed in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same Agreement. This Agreement may also be executed and delivered by facsimile signature and in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument.

19. **Headings.** The headings of the paragraphs of this Agreement are inserted for convenience only and shall not be deemed to constitute part of this Agreement or to affect the construction thereof

20. **Governing Law and Consent to Jurisdiction.** This Agreement and the legal relations among the parties shall be governed by, and construed and enforced in accordance with the laws of the State of Delaware, without regard to its conflict of laws rules. The Company and Indemnitee hereby irrevocably and unconditionally (i) agree that any action or proceeding arising out of or in connection with this Agreement shall be brought only in the Chancery Court of the State of Delaware (the **“Delaware Court”**), and not in any other state or federal court in the United States of America or any court in any other country, (ii) consent to submit to the exclusive jurisdiction of the Delaware Court for purposes of any action or proceeding arising out of or in connection with this Agreement, (iii) waive any objection to the laying of venue of any such action or proceeding in the Delaware Court, and (iv) waive, and agree not to plead or to

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make, any claim that any such action or proceeding brought in the Delaware Court has been brought in an improper or inconvenient forum.

**SIGNATURE PAGE TO FOLLOW**

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IN WITNESS WHEREOF, the parties hereto have executed this Indemnification Agreement on and as of the day and year first above written.

**PROTEON THERAPEUTICS, INC.**

By: /s/ Timothy Noyes  
Name: Timothy Noyes  
Title: President & CEO

**INDEMNITEE**

/s/ Hubert Birner

Name: Hubert Birner

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Address:  
TVM Capital  
Maximilianstrasse 35C  
80539 Munich  
Germany

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IN WITNESS WHEREOF, the parties hereto have executed this Indemnification Agreement on and as of the day and year first above written.

**PROTEON THERAPEUTICS, INC.**

By: \_\_\_\_\_

Name: \_\_\_\_\_

Title: \_\_\_\_\_

**INDEMNITEE**

\_\_\_\_\_  
Name: Hubert Birner

Address:  
TVM Capital  
Maximilianstrasse 35C  
80539 Munich  
Germany

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**INDEMNIFICATION AGREEMENT**

**INDEMNIFICATION AGREEMENT**

THIS INDEMNIFICATION AGREEMENT (the “**Agreement**”) is made and entered into as of September 10, 2012 between **PROTEON THERAPEUTICS, INC.**, a Delaware corporation (the “**Company**”), and Todd Foley (“**Indemnitee**”).

WITNESSETH THAT:

WHEREAS, highly competent persons have become more reluctant to serve corporations as directors or in other capacities unless they are provided with adequate protection through insurance or adequate indemnification against inordinate risks of claims and actions against them arising out of their service to and activities on behalf of the corporation;

WHEREAS, the Board of Directors of the Company (the “**Board**”) has determined that, in order to attract and retain qualified individuals, the Company will attempt to maintain on an ongoing basis, at its sole expense, liability insurance to protect persons serving the Company and its subsidiaries from certain liabilities. Although the furnishing of such insurance has been a customary and widespread practice among United States-based corporations and other business enterprises, the Company believes that, given current market conditions and trends, such insurance may be available to it in the future only at higher premiums and with more exclusions. At the same time, directors, officers, and other persons in service to corporations or business enterprises are being increasingly subjected to expensive and time-consuming litigation relating to, among other things, matters that traditionally would have been brought only against the Company or business enterprise itself. The Certificate of Incorporation of the Company permits, and the By-laws of the Company require, indemnification of directors of the Company. Indemnitee may also be entitled to indemnification pursuant to the General Corporation Law of the State of Delaware (“**DGCL**”). The By-laws and the DGCL expressly provide that the indemnification provisions set forth therein are not exclusive, and thereby contemplate that contracts may be entered into between the Company and members of the board of directors with respect to indemnification;

WHEREAS, the uncertainties relating to such insurance and to indemnification have increased the difficulty of attracting and retaining such persons;

WHEREAS, the Board has determined that the increased difficulty in attracting and retaining such persons is detrimental to the best interests of the Company’s stockholders and that the Company should act to assure such persons that there will be increased certainty of such protection in the future;

WHEREAS, it is reasonable, prudent and necessary for the Company contractually to obligate itself to indemnify, and to advance expenses on behalf of, such persons to the fullest extent permitted by applicable law so that they will serve or continue to serve the Company free from undue concern that they will not be so indemnified;

WHEREAS, this Agreement is a supplement to and in furtherance of the By-laws of the Company and any resolutions adopted pursuant thereto, and shall not be deemed a substitute therefor, nor to diminish or abrogate any rights of Indemnitee thereunder;

WHEREAS, Indemnitee does not regard the protection available under the Company’s By-laws and insurance as adequate in the present circumstances, and may not be willing to serve as a director without adequate protection, and the Company desires Indemnitee to serve in such capacity. Indemnitee is willing to serve, continue to serve and to take on additional service for or on behalf of the Company on the condition that he be so indemnified; and

NOW, THEREFORE, in consideration of Indemnitee’s agreement to serve as a director after the date hereof, the parties hereto agree as follows:

1. Indemnity of Indemnitee. The Company hereby agrees to hold harmless and indemnify Indemnitee to the fullest extent permitted by law, as such may be amended from time to time. In furtherance of the foregoing indemnification, and without limiting the generality thereof:

(a) Proceedings Other Than Proceedings by or in the Right of the Company. Indemnitee shall be entitled to the rights of indemnification provided in this Section 1(a) if, by reason of his Corporate Status (as hereinafter defined), the Indemnitee is, or is threatened to be made, a party to or participant in any Proceeding (as hereinafter defined) other than a Proceeding by or in the right of the Company. Pursuant to this Section 1(a), Indemnitee shall be indemnified against all Expenses (as hereinafter defined), judgments, penalties, fines and amounts paid in settlement actually and reasonably incurred by him, or on his behalf, in connection with such Proceeding or any claim, issue or matter therein, if the Indemnitee acted in good faith and in a manner the Indemnitee reasonably believed to be in or not opposed to the best interests of the Company, and with respect to any criminal Proceeding, had no reasonable cause to believe the Indemnitee’s conduct was unlawful.

(b) Proceedings by or in the Right of the Company. Indemnitee shall be entitled to the rights of indemnification provided in this Section 1(b) if, by reason of his Corporate Status, the Indemnitee is, or is threatened to be made, a party to or participant in any Proceeding brought by or in the right of the Company. Pursuant to this Section 1(b), Indemnitee shall be indemnified against all Expenses actually and reasonably incurred by the Indemnitee, or on the Indemnitee’s behalf, in connection with such Proceeding if the Indemnitee acted in good faith and in a manner the Indemnitee reasonably believed to be in or not opposed to the best interests of the Company; provided, however, if applicable law so provides, no indemnification against such Expenses shall be made in respect of any claim, issue or matter in such Proceeding as to which Indemnitee shall have been adjudged to be liable to the Company unless and to the extent that the Court of Chancery of the State of Delaware shall determine that such indemnification may be made.

(c) Indemnification for Expenses of a Party Who is Wholly or Partly Successful. Notwithstanding any other provision of this Agreement, to the extent that Indemnitee is, by reason of his Corporate Status, a party to and is successful, on the merits or otherwise, in any Proceeding, he shall be indemnified to the maximum extent permitted by law, as such may be amended from time to time, against all Expenses actually and reasonably incurred by him or on his behalf in connection therewith. If Indemnitee is not wholly successful in such Proceeding but is successful, on the merits or otherwise, as to one or more but less than all claims, issues or matters in such Proceeding, the Company shall indemnify Indemnitee against all Expenses actually and reasonably incurred by him or on his behalf in connection with each successfully resolved claim, issue or matter. For purposes of this Section and without

limitation, the termination of any claim, issue or matter in such a Proceeding by dismissal, with or without prejudice, shall be deemed to be a successful result as to such claim, issue or matter.

2. Additional Indemnity. In addition to, and without regard to any limitations on, the indemnification provided for in Section 1 of this Agreement, the Company shall and hereby does indemnify and hold harmless Indemnitee against all Expenses, judgments, penalties, fines and amounts paid in settlement actually and reasonably incurred by him or on his behalf if, by reason of his Corporate Status, he is, or is threatened to be made, a party to or participant in any Proceeding (including a Proceeding by or in the right of the Company), including, without limitation, all liability arising out of the negligence or active or passive wrongdoing of Indemnitee. The only limitation that shall exist upon the Company's obligations pursuant to this Agreement shall be that the Company shall not be obligated to make any payment to Indemnitee that is finally determined (under the procedures, and subject to the presumptions, set forth in Sections 6 and 7 hereof) to be unlawful.

3. Contribution.

(a) Whether or not the indemnification provided in Sections 1 and 2 hereof is available, in respect of any threatened, pending or completed action, suit or proceeding in which the Company is jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding), the Company shall pay, in the first instance, the entire amount of any judgment or settlement of such action, suit or proceeding without requiring Indemnitee to contribute to such payment and the Company hereby waives and relinquishes any right of contribution it may have against Indemnitee. The Company shall not enter into any settlement of any action, suit or proceeding in which the Company is jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding) unless such settlement provides for a full and final release of all claims asserted against Indemnitee.

(b) Without diminishing or impairing the obligations of the Company set forth in the preceding subparagraph, if, for any reason, Indemnitee shall elect or be required to pay all or any portion of any judgment or settlement in any threatened, pending or completed action, suit or proceeding in which the Company is jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding), the Company shall contribute to the amount of expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred and paid or payable by Indemnitee in proportion to the relative benefits received by the Company and all officers, directors or employees of the Company, other than Indemnitee, who are jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding), on the one hand, and Indemnitee, on the other hand, from the transaction from which such action, suit or proceeding arose; provided, however, that the proportion determined on the basis of relative benefit may, to the extent necessary to conform to law, be further adjusted by reference to the relative fault of the Company and all officers, directors or employees of the Company other than Indemnitee who are jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding), on the one hand, and Indemnitee, on the other hand, in connection with the events that resulted in such expenses, judgments, fines or settlement amounts, as well as any other equitable considerations which the Law may require to be considered. The relative fault of the Company and all officers, directors or employees of the Company, other than Indemnitee, who are jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding), on the one hand, and Indemnitee, on the other hand, shall be determined by reference to, among other things, the degree to which their actions were motivated

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by intent to gain personal profit or advantage, the degree to which their liability is primary or secondary and the degree to which their conduct is active or passive.

(c) The Company hereby agrees to fully indemnify and hold Indemnitee harmless from any claims of contribution which may be brought by officers, directors or employees of the Company, other than Indemnitee, who may be jointly liable with Indemnitee.

(d) To the fullest extent permissible under applicable law, if the indemnification provided for in this Agreement is unavailable to Indemnitee for any reason whatsoever, the Company, in lieu of indemnifying Indemnitee, shall contribute to the amount incurred by Indemnitee, whether for judgments, fines, penalties, excise taxes, amounts paid or to be paid in settlement and/or for Expenses, in connection with any claim relating to an indemnifiable event under this Agreement, in such proportion as is deemed fair and reasonable in light of all of the circumstances of such Proceeding in order to reflect (i) the relative benefits received by the Company and Indemnitee as a result of the event(s) and/or transaction(s) giving cause to such Proceeding; and/or (ii) the relative fault of the Company (and its directors, officers, employees and agents) and Indemnitee in connection with such event(s) and/or transaction(s).

4. Indemnification for Expenses of a Witness. Notwithstanding any other provision of this Agreement, to the extent that Indemnitee is, by reason of his Corporate Status, a witness in any Proceeding to which Indemnitee is not a party, he shall be indemnified against all Expenses actually and reasonably incurred by him or on his behalf in connection therewith.

5. Advancement of Expenses. Notwithstanding any other provision of this Agreement, the Company shall advance all Expenses incurred by or on behalf of Indemnitee in connection with any Proceeding by reason of Indemnitee's Corporate Status within thirty (30) days after the receipt by the Company of a statement or statements from Indemnitee requesting such advance or advances from time to time, whether prior to or after final disposition of such Proceeding. Such statement or statements shall reasonably evidence the Expenses incurred by Indemnitee and shall include or be preceded or accompanied by an undertaking by or on behalf of Indemnitee to repay any Expenses advanced if it shall ultimately be determined that Indemnitee is not entitled to be indemnified against such Expenses. Any advances and undertakings to repay pursuant to this Section 5 shall be unsecured and interest free.

6. Procedures and Presumptions for Determination of Entitlement to Indemnification. It is the intent of this Agreement to secure for Indemnitee rights of indemnity that are as favorable as may be permitted under the Delaware General Corporation Law and public policy of the State of Delaware. Accordingly, the parties agree that the following procedures and presumptions shall apply in the event of any question as to whether Indemnitee is entitled to indemnification under this Agreement:

(a) To obtain indemnification under this Agreement, Indemnitee shall submit to the Company a written request, including therein or therewith such documentation and information as is reasonably available to Indemnitee and is reasonably necessary to determine whether and to what extent Indemnitee is entitled to indemnification. The Secretary of the Company shall, promptly upon receipt of such a request for indemnification, advise the Board of Directors in writing that Indemnitee has requested indemnification.

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(b) Upon written request by Indemnitee for indemnification pursuant to the first sentence of Section 6(a) hereof, a determination, if required by applicable law, with respect to Indemnitee's entitlement thereto shall be made in the specific case by one of the following three methods, which shall be

at the election of the board: (1) by a majority vote of the disinterested directors, even though less than a quorum, by a committee of disinterested directors designated by a majority vote of the disinterested directors, even though less than a quorum, (2) if there are no disinterested directors or if the disinterested directors so direct, by independent legal counsel in a written opinion to the Board of Directors, a copy of which shall be delivered to the Indemnitee, or (3) if so directed by the Board of Directors, by the stockholders of the Company. For purposes hereof, disinterested directors are those members of the board of directors of the Company who are not parties to the action, suit or proceeding in respect of which indemnification is sought by Indemnitee.

(c) If the determination of entitlement to indemnification is to be made by Independent Counsel pursuant to Section 6(b) hereof, the Independent Counsel shall be selected as provided in this Section 6(c). The determination of whether Independent Counsel shall be engaged and the selection of such Independent Counsel shall be made by the Board of Directors. Indemnitee may, within 10 days after such written notice of selection shall have been given, deliver to the Company, as the case may be, a written objection to such selection; provided, however, that such objection may be asserted only on the ground that the Independent Counsel so selected does not meet the requirements of “**Independent Counsel**” as defined in Section 13 of this Agreement, and the objection shall set forth with particularity the factual basis of such assertion. Absent a proper and timely objection, the person so selected shall act as Independent Counsel. If a written objection is made and substantiated, the Independent Counsel selected may not serve as Independent Counsel unless and until such objection is withdrawn or a court has determined that such objection is without merit. If, within 20 days after submission by Indemnitee of a written request for indemnification pursuant to Section 6(a) hereof, no Independent Counsel shall have been selected and not objected to, either the Company or Indemnitee may petition the Court of Chancery of the State of Delaware or other court of competent jurisdiction for resolution of any objection which shall have been made by the Indemnitee to the Company’s selection of Independent Counsel and/or for the appointment as Independent Counsel of a person selected by the court or by such other person as the court shall designate, and the person with respect to whom all objections are so resolved or the person so appointed shall act as Independent Counsel under Section 6(b) hereof. The Company shall pay any and all reasonable fees and expenses of Independent Counsel incurred by such Independent Counsel in connection with acting pursuant to Section 6(b) hereof, and the Company shall pay all reasonable fees and expenses incident to the procedures of this Section 6(c), regardless of the manner in which such Independent Counsel was selected or appointed.

(d) In making a determination with respect to entitlement to indemnification hereunder, the person or persons or entity making such determination shall presume that Indemnitee is entitled to indemnification under this Agreement. Anyone seeking to overcome this presumption shall have the burden of proof and the burden of persuasion by clear and convincing evidence. Neither the failure of the Company (including by its directors or independent legal counsel) to have made a determination prior to the commencement of any action pursuant to this Agreement that indemnification is proper in the circumstances because Indemnitee has met the applicable standard of conduct, nor an actual determination by the Company (including by its directors or independent legal counsel) that Indemnitee has not met

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such applicable standard of conduct, shall be a defense to the action or create a presumption that Indemnitee has not met the applicable standard of conduct.

(e) Indemnitee shall be deemed to have acted in good faith if Indemnitee’s action is based on the records or books of account of the Enterprise (as hereinafter defined), including financial statements, or on information supplied to Indemnitee by the officers of the Enterprise in the course of their duties, or on the advice of legal counsel for the Enterprise or on information or records given or reports made to the Enterprise by an independent certified public accountant or by an appraiser or other expert selected with reasonable care by the Enterprise. In addition, the knowledge and/or actions, or failure to act, of any director, officer, agent or employee of the Enterprise shall not be imputed to Indemnitee for purposes of determining the right to indemnification under this Agreement. Whether or not the foregoing provisions of this Section 6(e) are satisfied, it shall in any event be presumed that Indemnitee has at all times acted in good faith and in a manner he reasonably believed to be in or not opposed to the best interests of the Company. Anyone seeking to overcome this presumption shall have the burden of proof and the burden of persuasion by clear and convincing evidence.

(f) If the person, persons or entity empowered or selected under Section 6 to determine whether Indemnitee is entitled to indemnification shall not have made a determination within sixty (60) days after receipt by the Company of the request therefor, the requisite determination of entitlement to indemnification shall be deemed to have been made and Indemnitee shall be entitled to such indemnification absent (i) a misstatement by Indemnitee of a material fact, or an omission of a material fact necessary to make Indemnitee’s statement not materially misleading, in connection with the request for indemnification, or (ii) a prohibition of such indemnification under applicable law; provided, however, that such 60-day period may be extended for a reasonable time, not to exceed an additional thirty (30) days, if the person, persons or entity making such determination with respect to entitlement to indemnification in good faith requires such additional time to obtain or evaluate documentation and/or information relating thereto; and provided, further, that the foregoing provisions of this Section 6(f) shall not apply if the determination of entitlement to indemnification is to be made by the stockholders pursuant to Section 6(b) of this Agreement and if (A) within fifteen (15) days after receipt by the Company of the request for such determination, the Board of Directors or the Disinterested Directors, if appropriate, resolve to submit such determination to the stockholders for their consideration at an annual meeting thereof to be held within seventy-five (75) days after such receipt and such determination is made thereat, or (B) a special meeting of stockholders is called within fifteen (15) days after such receipt for the purpose of making such determination, such meeting is held for such purpose within sixty (60) days after having been so called and such determination is made thereat.

(g) Indemnitee shall cooperate with the person, persons or entity making such determination with respect to Indemnitee’s entitlement to indemnification, including providing to such person, persons or entity upon reasonable advance request any documentation or information which is not privileged or otherwise protected from disclosure and which is reasonably available to Indemnitee and reasonably necessary to such determination. Any Independent Counsel, member of the Board of Directors or stockholder of the Company shall act reasonably and in good faith in making a determination regarding the Indemnitee’s entitlement to indemnification under this Agreement. Any costs or expenses (including attorneys’ fees and disbursements) incurred by Indemnitee in so cooperating with the person, persons or entity making such determination shall be borne by the Company (irrespective of the

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determination as to Indemnitee’s entitlement to indemnification) and the Company hereby indemnifies and agrees to hold Indemnitee harmless therefrom.

(h) The Company acknowledges that a settlement or other disposition short of final judgment may be successful if it permits a party to avoid expense, delay, distraction, disruption and uncertainty. In the event that any action, claim or proceeding to which Indemnitee is a party is resolved in any manner other than by adverse judgment against Indemnitee (including, without limitation, settlement of such action, claim or proceeding with or without payment of money or other consideration) it shall be presumed that Indemnitee has been successful on the merits or otherwise in such action, suit or proceeding. Anyone seeking to overcome this presumption shall have the burden of proof and the burden of persuasion by clear and convincing evidence.

(i) The termination of any Proceeding or of any claim, issue or matter therein, by judgment, order, settlement or conviction, or upon a plea of nolo contendere or its equivalent, shall not (except as otherwise expressly provided in this Agreement) of itself adversely affect the right of Indemnitee to

indemnification or create a presumption that Indemnitee did not act in good faith and in a manner which he reasonably believed to be in or not opposed to the best interests of the Company or, with respect to any criminal Proceeding, that Indemnitee had reasonable cause to believe that his conduct was unlawful.

7. Remedies of Indemnitee.

(a) In the event that (i) a determination is made pursuant to Section 6 of this Agreement that Indemnitee is not entitled to indemnification under this Agreement, (ii) advancement of Expenses is not timely made pursuant to Section 5 of this Agreement, (iii) no determination of entitlement to indemnification is made pursuant to Section 6(b) of this Agreement within 90 days after receipt by the Company of the request for indemnification, (iv) payment of indemnification is not made pursuant to this Agreement within ten (10) days after receipt by the Company of a written request therefor or (v) payment of indemnification is not made within ten (10) days after a determination has been made that Indemnitee is entitled to indemnification or such determination is deemed to have been made pursuant to Section 6 of this Agreement, Indemnitee shall be entitled to an adjudication in an appropriate court of the State of Delaware, or in any other court of competent jurisdiction, of Indemnitee's entitlement to such indemnification. Indemnitee shall commence such proceeding seeking an adjudication within 180 days following the date on which Indemnitee first has the right to commence such proceeding pursuant to this Section 7(a). The Company shall not oppose Indemnitee's right to seek any such adjudication.

(b) In the event that a determination shall have been made pursuant to Section 6(b) of this Agreement that Indemnitee is not entitled to indemnification, any judicial proceeding commenced pursuant to this Section 7 shall be conducted in all respects as a de novo trial on the merits, and Indemnitee shall not be prejudiced by reason of the adverse determination under Section 6(b).

(c) If a determination shall have been made pursuant to Section 6(b) of this Agreement that Indemnitee is entitled to indemnification, the Company shall be bound by such determination in any judicial proceeding commenced pursuant to this Section 7 absent (i) a misstatement by Indemnitee of a material fact, or an omission of a material fact necessary to

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make Indemnitee's statement not materially misleading in connection with the application for indemnification, or (ii) a prohibition of such indemnification under applicable law.

(d) In the event that Indemnitee, pursuant to this Section 7, seeks a judicial adjudication of his rights under, or to recover damages for breach of, this Agreement, or to recover under any directors' and officers' liability insurance policies maintained by the Company, the Company shall pay on his behalf, in advance, any and all expenses (of the types described in the definition of Expenses in Section 13 of this Agreement) actually and reasonably incurred by him in such judicial adjudication, regardless of whether Indemnitee ultimately is determined to be entitled to such indemnification, advancement of expenses or insurance recovery.

(e) The Company shall be precluded from asserting in any judicial proceeding commenced pursuant to this Section 7 that the procedures and presumptions of this Agreement are not valid, binding and enforceable and shall stipulate in any such court that the Company is bound by all the provisions of this Agreement. The Company shall indemnify Indemnitee against any and all Expenses and, if requested by Indemnitee, shall (within ten (10) days after receipt by the Company of a written request therefore) advance, to the extent not prohibited by law, such expenses to Indemnitee, which are incurred by Indemnitee in connection with any action brought by Indemnitee for indemnification or advance of Expenses from the Company under this Agreement or under any directors' and officers' liability insurance policies maintained by the Company, regardless of whether Indemnitee ultimately is determined to be entitled to such indemnification, advancement of Expenses or insurance recovery, as the case may be.

(f) Notwithstanding anything in this Agreement to the contrary, no determination as to entitlement to indemnification under this Agreement shall be required to be made prior to the final disposition of the Proceeding.

8. Non-Exclusivity; Survival of Rights; Insurance; Subrogation.

(a) The rights of indemnification as provided by this Agreement shall not be deemed exclusive of any other rights to which Indemnitee may at any time be entitled under applicable law, the certificate of incorporation of the Company, the Bylaws, any agreement, a vote of stockholders, a resolution of directors or otherwise. No amendment, alteration or repeal of this Agreement or of any provision hereof shall limit or restrict any right of Indemnitee under this Agreement in respect of any action taken or omitted by such Indemnitee in his Corporate Status prior to such amendment, alteration or repeal. To the extent that a change in the Delaware General Corporation Law, whether by statute or judicial decision, permits greater indemnification than would be afforded currently under the Bylaws and this Agreement, it is the intent of the parties hereto that Indemnitee shall enjoy by this Agreement the greater benefits so afforded by such change. No right or remedy herein conferred is intended to be exclusive of any other right or remedy, and every other right and remedy shall be cumulative and in addition to every other right and remedy given hereunder or now or hereafter existing at law or in equity or otherwise. The assertion or employment of any right or remedy hereunder, or otherwise, shall not prevent the concurrent assertion or employment of any other right or remedy.

(b) To the extent that the Company maintains an insurance policy or policies providing liability insurance for directors, officers, employees, or agents or fiduciaries of

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the Company or of any other corporation, partnership, joint venture, trust, employee benefit plan or other enterprise that such person serves at the request of the Company, Indemnitee shall be covered by such policy or policies in accordance with its or their terms to the maximum extent of the coverage available for any director, officer, employee, agent or fiduciary under such policy or policies. If, at the time of the receipt of a notice of a claim pursuant to the terms hereof, the Company has director and officer liability insurance in effect, the Company shall give prompt notice of the commencement of such proceeding to the insurers in accordance with the procedures set forth in the respective policies. The Company shall thereafter take all necessary or desirable action to cause such insurers to pay, on behalf of the Indemnitee, all amounts payable as a result of such proceeding in accordance with the terms of such policies.

(c) In the event of any payment under this Agreement, the Company shall be subrogated to the extent of such payment to all of the rights of recovery of Indemnitee, who shall execute all papers required and take all action necessary to secure such rights, including execution of such documents as are necessary to enable the Company to bring suit to enforce such rights.

(d) The Company shall not be liable under this Agreement to make any payment of amounts otherwise indemnifiable hereunder if and to the extent that Indemnitee has otherwise actually received such payment under any insurance policy, contract, agreement or otherwise.

(e) The Company's obligation to indemnify or advance Expenses hereunder to Indemnitee who is or was serving at the request of the Company as a director, officer, employee or agent of any other corporation, partnership, joint venture, trust, employee benefit plan or other enterprise shall be reduced by any amount Indemnitee has actually received as indemnification or advancement of expenses from such other corporation, partnership, joint venture, trust, employee benefit plan or other enterprise.

9. Exception to Right of Indemnification. Notwithstanding any provision in this Agreement, the Company shall not be obligated under this Agreement to make any indemnity in connection with any claim made against Indemnitee:

(a) for which payment has actually been made to or on behalf of Indemnitee under any insurance policy or other indemnity provision, except with respect to any excess beyond the amount paid under any insurance policy or other indemnity provision; or

(b) for an accounting of profits made from the purchase and sale (or sale and purchase) by Indemnitee of securities of the Company within the meaning of Section 16(b) of the Securities Exchange Act of 1934, as amended, or similar provisions of state statutory law or common law; or

(c) in connection with any Proceeding (or any part of any Proceeding) initiated by Indemnitee, including any Proceeding (or any part of any Proceeding) initiated by Indemnitee against the Company or its directors, officers, employees or other indemnitees, unless (i) the Board of Directors of the Company authorized the Proceeding (or any part of any Proceeding) prior to its initiation or (ii) the Company provides the indemnification, in its sole discretion, pursuant to the powers vested in the Company under applicable law.

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10. Duration of Agreement. All agreements and obligations of the Company contained herein shall continue during the period Indemnitee is a director of the Company (or is or was serving at the request of the Company as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise) and for a period of five (5) years thereafter, and in addition shall continue thereafter so long as Indemnitee shall be subject to any Proceeding (or any proceeding commenced under Section 7 hereof) by reason of his Corporate Status, whether or not he is acting or serving in any such capacity at the time any liability or expense is incurred for which indemnification can be provided under this Agreement. This Agreement shall be binding upon and inure to the benefit of and be enforceable by the parties hereto and their respective successors (including any direct or indirect successor by purchase, merger, consolidation or otherwise to all or substantially all of the business or assets of the Company), assigns, spouses, heirs, executors and personal and legal representatives.

11. Security. To the extent requested by Indemnitee and approved by the Board of Directors of the Company, the Company may at any time and from time to time provide security to Indemnitee for the Company's obligations hereunder through an irrevocable bank line of credit, funded trust or other collateral. Any such security, once provided to Indemnitee, may not be revoked or released without the prior written consent of the Indemnitee.

12. Enforcement.

(a) The Company expressly confirms and agrees that it has entered into this Agreement and assumes the obligations imposed on it hereby in order to induce Indemnitee to serve as a director of the Company, and the Company acknowledges that Indemnitee is relying upon this Agreement in serving as a director of the Company.

(b) This Agreement constitutes the entire agreement between the parties hereto with respect to the subject matter hereof and supersedes all prior agreements and understandings, oral, written and implied, between the parties hereto with respect to the subject matter hereof.

13. Definitions. For purposes of this Agreement:

(a) "**Corporate Status**" describes the status of a person who is or was a director, officer, employee, agent or fiduciary of the Company or of any other corporation, partnership, joint venture, trust, employee benefit plan or other enterprise that such person is or was serving at the express written request of the Company.

(b) "**Disinterested Director**" means a director of the Company who is not and was not a party to the Proceeding in respect of which indemnification is sought by Indemnitee.

(c) "**Enterprise**" shall mean the Company and any other corporation, partnership, joint venture, trust, employee benefit plan or other enterprise that Indemnitee is or was serving at the express written request of the Company as a director, officer, employee, agent or fiduciary.

(d) "**Expenses**" shall include all reasonable attorneys' fees, retainers, court costs, transcript costs, fees of experts, witness fees, travel expenses, duplicating costs,

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printing and binding costs, telephone charges, postage, delivery service fees and all other disbursements or expenses of the types customarily incurred in connection with prosecuting, defending, preparing to prosecute or defend, investigating, participating, or being or preparing to be a witness in a Proceeding. Expenses also shall include Expenses incurred in connection with any appeal resulting from any Proceeding, including without limitation the premium, security for, and other costs relating to any cost bond, supersedeas bond, or other appeal bond or its equivalent. Expenses, however, shall not include amounts paid in settlement by Indemnitee or the amount of judgments or fines against Indemnitee.

(e) "**Independent Counsel**" means a law firm, or a member of a law firm, that is experienced in matters of corporation law and neither presently is, nor in the past five years has been, retained to represent: (i) the Company or Indemnitee in any matter material to either such party (other than with respect to matters concerning Indemnitee under this Agreement, or of other indemnitees under similar indemnification agreements), or (ii) any other party to the Proceeding giving rise to a claim for indemnification hereunder. Notwithstanding the foregoing, the term "Independent Counsel" shall not include any person who, under the applicable standards of professional conduct then prevailing, would have a conflict of interest in representing either the Company or Indemnitee in an action to determine Indemnitee's rights under this Agreement. The Company agrees to pay the reasonable fees of the Independent Counsel referred to above and to fully indemnify such counsel against any and all Expenses, claims, liabilities and damages arising out of or relating to this Agreement or its engagement pursuant hereto.



(f) **“Proceeding”** includes any threatened, pending or completed action, suit, arbitration, alternate dispute resolution mechanism, investigation, inquiry, administrative hearing or any other actual, threatened or completed proceeding, whether brought by or in the right of the Company or otherwise and whether civil, criminal, administrative or investigative, in which Indemnitee was, is or will be involved as a party or otherwise, by reason of the fact that Indemnitee is or was a director of the Company, by reason of any action taken by him or of any inaction on his part while acting as a director of the Company, or by reason of the fact that he is or was serving at the request of the Company as a director, officer, employee, agent or fiduciary of another corporation, partnership, joint venture, trust or other Enterprise; in each case whether or not he is acting or serving in any such capacity at the time any liability or expense is incurred for which indemnification can be provided under this Agreement; including one pending on or before the date of this Agreement, but excluding one initiated by an Indemnitee pursuant to Section 7 of this Agreement to enforce his rights under this Agreement.

14. **Severability.** The invalidity of unenforceability of any provision hereof shall in no way affect the validity or enforceability of any other provision. Without limiting the generality of the foregoing, this Agreement is intended to confer upon Indemnitee indemnification rights to the fullest extent permitted by applicable laws. In the event any provision hereof conflicts with any applicable law, such provision shall be deemed modified, consistent with the aforementioned intent, to the extent necessary to resolve such conflict.

15. **Modification and Waiver.** No supplement, modification, termination or amendment of this Agreement shall be binding unless executed in writing by both of the parties hereto. No waiver of any of the provisions of this Agreement shall be deemed or shall constitute a waiver of any other provisions hereof (whether or not similar) nor shall such waiver constitute a continuing waiver.

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16. **Notice By Indemnitee.** Indemnitee agrees promptly to notify the Company in writing upon being served with or otherwise receiving any summons, citation, subpoena, complaint, indictment, information or other document relating to any Proceeding or matter which may be subject to indemnification covered hereunder. The failure to so notify the Company shall not relieve the Company of any obligation which it may have to Indemnitee under this Agreement or otherwise unless and only to the extent that such failure or delay materially prejudices the Company.

17. **Notices.** All notices and other communications given or made pursuant to this Agreement shall be in writing and shall be deemed effectively given: (a) upon personal delivery to the party to be notified, (b) when sent by confirmed electronic mail or facsimile if sent during normal business hours of the recipient, and if not so confirmed, then on the next business day, (c) five (5) days after having been sent by registered or certified mail, return receipt requested, postage prepaid, or (d) one (1) day after deposit with a nationally recognized overnight courier, specifying next day delivery, with written verification of receipt. All communications shall be sent:

(a) To Indemnitee at the address set forth below Indemnitee’s signature hereto.

(b) To the Company at:

200 West Street  
Waltham, MA 02451  
Attention: CEO

or to such other address as may have been furnished to Indemnitee by the Company or to the Company by Indemnitee, as the case may be.

18. **Counterparts.** This Agreement may be executed in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same Agreement. This Agreement may also be executed and delivered by facsimile signature and in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument.

19. **Headings.** The headings of the paragraphs of this Agreement are inserted for convenience only and shall not be deemed to constitute part of this Agreement or to affect the construction thereof.

20. **Governing Law and Consent to Jurisdiction.** This Agreement and the legal relations among the parties shall be governed by, and construed and enforced in accordance with, the laws of the State of Delaware, without regard to its conflict of laws rules. The Company and Indemnitee hereby irrevocably and unconditionally (i) agree that any action or proceeding arising out of or in connection with this Agreement shall be brought only in the Chancery Court of the State of Delaware (the **“Delaware Court”**), and not in any other state or federal court in the United States of America or any court in any other country, (ii) consent to submit to the exclusive jurisdiction of the Delaware Court for purposes of any action or proceeding arising out of or in connection with this Agreement, (iii) waive any objection to the laying of venue of any such action or proceeding in the Delaware Court, and (iv) waive, and agree not to plead or to

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make, any claim that any such action or proceeding brought in the Delaware Court has been brought in an improper or inconvenient forum.

**SIGNATURE PAGE TO FOLLOW**

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IN WITNESS WHEREOF, the parties hereto have executed this Indemnification Agreement on and as of the day and year first above written.

**PROTEON THERAPEUTICS, INC.**

By: \_\_\_\_\_  
Name: \_\_\_\_\_  
Title: \_\_\_\_\_

**INDEMNITEE**

/s/ Todd Foley

Name: Todd Foley

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Address:

78 Dean Rd

Brookline, MA 02445

**SIGNATURE PAGE TO INDEMNIFICATION AGREEMENT - FOLEY**

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**INDEMNIFICATION AGREEMENT**

**INDEMNIFICATION AGREEMENT**

THIS INDEMNIFICATION AGREEMENT (the “**Agreement**”) is made and entered into as of February 6, 2013 between **PROTEON THERAPEUTICS, INC.**, a Delaware corporation (the “**Company**”), and Timothy P. Noyes (“**Indemnitee**”).

WITNESSETH THAT:

WHEREAS, highly competent persons have become more reluctant to serve corporations as directors or in other capacities unless they are provided with adequate protection through insurance or adequate indemnification against inordinate risks of claims and actions against them arising out of their service to and activities on behalf of the corporation;

WHEREAS, the Board of Directors of the Company (the “**Board**”) has determined that, in order to attract and retain qualified individuals, the Company will attempt to maintain on an ongoing basis, at its sole expense, liability insurance to protect persons serving the Company and its subsidiaries from certain liabilities. Although the furnishing of such insurance has been a customary and widespread practice among United States-based corporations and other business enterprises, the Company believes that, given current market conditions and trends, such insurance may be available to it in the future only at higher premiums and with more exclusions. At the same time, directors, officers, and other persons in service to corporations or business enterprises are being increasingly subjected to expensive and time-consuming litigation relating to, among other things, matters that traditionally would have been brought only against the Company or business enterprise itself. The Certificate of Incorporation of the Company permits, and the By-laws of the Company require, indemnification of directors of the Company. Indemnitee may also be entitled to indemnification pursuant to the General Corporation Law of the State of Delaware (“**DGCL**”). The By-laws and the DGCL expressly provide that the indemnification provisions set forth therein are not exclusive, and thereby contemplate that contracts may be entered into between the Company and members of the board of directors with respect to indemnification;

WHEREAS, the uncertainties relating to such insurance and to indemnification have increased the difficulty of attracting and retaining such persons;

WHEREAS, the Board has determined that the increased difficulty in attracting and retaining such persons is detrimental to the best interests of the Company’s stockholders and that the Company should act to assure such persons that there will be increased certainty of such protection in the future;

WHEREAS, it is reasonable, prudent and necessary for the Company contractually to obligate itself to indemnify, and to advance expenses on behalf of, such persons to the fullest extent permitted by applicable law so that they will serve or continue to serve the Company free from undue concern that they will not be so indemnified;

WHEREAS, this Agreement is a supplement to and in furtherance of the By-laws of the Company and any resolutions adopted pursuant thereto, and shall not be deemed a substitute therefor, nor to diminish or abrogate any rights of Indemnitee thereunder;

WHEREAS, Indemnitee does not regard the protection available under the Company’s By-laws and insurance as adequate in the present circumstances, and may not be willing to serve as a director without adequate protection, and the Company desires Indemnitee to serve in such capacity. Indemnitee is willing to serve, continue to serve and to take on additional service for or on behalf of the Company on the condition that he be so indemnified; and

NOW, THEREFORE, in consideration of Indemnitee’s agreement to serve as a director after the date hereof, the parties hereto agree as follows:

1. Indemnity of Indemnitee. The Company hereby agrees to hold harmless and indemnify Indemnitee to the fullest extent permitted by law, as such may be amended from time to time. In furtherance of the foregoing indemnification, and without limiting the generality thereof:

(a) Proceedings Other Than Proceedings by or in the Right of the Company. Indemnitee shall be entitled to the rights of indemnification provided in this Section 1(a) if, by reason of his Corporate Status (as hereinafter defined), the Indemnitee is, or is threatened to be made, a party to or participant in any Proceeding (as hereinafter defined) other than a Proceeding by or in the right of the Company. Pursuant to this Section 1(a), Indemnitee shall be indemnified against all Expenses (as hereinafter defined), judgments, penalties, fines and amounts paid in settlement actually and reasonably incurred by him, or on his behalf, in connection with such Proceeding or any claim, issue or matter therein, if the Indemnitee acted in good faith and in a manner the Indemnitee reasonably believed to be in or not opposed to the best interests of the Company, and with respect to any criminal Proceeding, had no reasonable cause to believe the Indemnitee’s conduct was unlawful.

(b) Proceedings by or in the Right of the Company. Indemnitee shall be entitled to the rights of indemnification provided in this Section 1(b) if, by reason of his Corporate Status, the Indemnitee is, or is threatened to be made, a party to or participant in any Proceeding brought by or in the right of the Company. Pursuant to this Section 1(b), Indemnitee shall be indemnified against all Expenses actually and reasonably incurred by the Indemnitee, or on the Indemnitee’s behalf, in connection with such Proceeding if the Indemnitee acted in good faith and in a manner the Indemnitee reasonably believed to be in or not opposed to the best interests of the Company; provided, however, if applicable law so provides, no indemnification against such Expenses shall be made in respect of any claim, issue or matter in such Proceeding as to which Indemnitee shall have been adjudged to be liable to the Company unless and to the extent that the Court of Chancery of the State of Delaware shall determine that such indemnification may be made.

(c) Indemnification for Expenses of a Party Who is Wholly or Partly Successful. Notwithstanding any other provision of this Agreement, to the extent that Indemnitee is, by reason of his Corporate Status, a party to and is successful, on the merits or otherwise, in any Proceeding, he shall be indemnified to the maximum extent permitted by law, as such may be amended from time to time, against all Expenses actually and reasonably incurred by him or on his behalf in connection therewith. If Indemnitee is not wholly successful in such Proceeding but is successful, on the merits or otherwise, as to one or more but less than all claims, issues or matters in such Proceeding, the Company shall indemnify Indemnitee against all Expenses actually and reasonably incurred by him or on his behalf in connection with each successfully resolved claim, issue or matter. For purposes of this Section and without

limitation, the termination of any claim, issue or matter in such a Proceeding by dismissal, with or without prejudice, shall be deemed to be a successful result as to such claim, issue or matter.

2. Additional Indemnity. In addition to, and without regard to any limitations on, the indemnification provided for in Section 1 of this Agreement, the Company shall and hereby does indemnify and hold harmless Indemnitee against all Expenses, judgments, penalties, fines and amounts paid in settlement actually and reasonably incurred by him or on his behalf if, by reason of his Corporate Status, he is, or is threatened to be made, a party to or participant in any Proceeding (including a Proceeding by or in the right of the Company), including, without limitation, all liability arising out of the negligence or active or passive wrongdoing of Indemnitee. The only limitation that shall exist upon the Company's obligations pursuant to this Agreement shall be that the Company shall not be obligated to make any payment to Indemnitee that is finally determined (under the procedures, and subject to the presumptions, set forth in Sections 6 and 7 hereof) to be unlawful.

3. Contribution.

(a) Whether or not the indemnification provided in Sections 1 and 2 hereof is available, in respect of any threatened, pending or completed action, suit or proceeding in which the Company is jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding), the Company shall pay, in the first instance, the entire amount of any judgment or settlement of such action, suit or proceeding without requiring Indemnitee to contribute to such payment and the Company hereby waives and relinquishes any right of contribution it may have against Indemnitee. The Company shall not enter into any settlement of any action, suit or proceeding in which the Company is jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding) unless such settlement provides for a full and final release of all claims asserted against Indemnitee.

(b) Without diminishing or impairing the obligations of the Company set forth in the preceding subparagraph, if, for any reason, Indemnitee shall elect or be required to pay all or any portion of any judgment or settlement in any threatened, pending or completed action, suit or proceeding in which the Company is jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding), the Company shall contribute to the amount of expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred and paid or payable by Indemnitee in proportion to the relative benefits received by the Company and all officers, directors or employees of the Company, other than Indemnitee, who are jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding), on the one hand, and Indemnitee, on the other hand, from the transaction from which such action, suit or proceeding arose; provided, however, that the proportion determined on the basis of relative benefit may, to the extent necessary to conform to law, be further adjusted by reference to the relative fault of the Company and all officers, directors or employees of the Company other than Indemnitee who are jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding), on the one hand, and Indemnitee, on the other hand, in connection with the events that resulted in such expenses, judgments, fines or settlement amounts, as well as any other equitable considerations which the Law may require to be considered. The relative fault of the Company and all officers, directors or employees of the Company, other than Indemnitee, who are jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding), on the one hand, and Indemnitee, on the other hand, shall be determined by reference to, among other things, the degree to which their actions were motivated

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by intent to gain personal profit or advantage, the degree to which their liability is primary or secondary and the degree to which their conduct is active or passive.

(c) The Company hereby agrees to fully indemnify and hold Indemnitee harmless from any claims of contribution which may be brought by officers, directors or employees of the Company, other than Indemnitee, who may be jointly liable with Indemnitee.

(d) To the fullest extent permissible under applicable law, if the indemnification provided for in this Agreement is unavailable to Indemnitee for any reason whatsoever, the Company, in lieu of indemnifying Indemnitee, shall contribute to the amount incurred by Indemnitee, whether for judgments, fines, penalties, excise taxes, amounts paid or to be paid in settlement and/or for Expenses, in connection with any claim relating to an indemnifiable event under this Agreement, in such proportion as is deemed fair and reasonable in light of all of the circumstances of such Proceeding in order to reflect (i) the relative benefits received by the Company and Indemnitee as a result of the event(s) and/or transaction(s) giving cause to such Proceeding; and/or (ii) the relative fault of the Company (and its directors, officers, employees and agents) and Indemnitee in connection with such event(s) and/or transaction(s).

4. Indemnification for Expenses of a Witness. Notwithstanding any other provision of this Agreement, to the extent that Indemnitee is, by reason of his Corporate Status, a witness in any Proceeding to which Indemnitee is not a party, he shall be indemnified against all Expenses actually and reasonably incurred by him or on his behalf in connection therewith.

5. Advancement of Expenses. Notwithstanding any other provision of this Agreement, the Company shall advance all Expenses incurred by or on behalf of Indemnitee in connection with any Proceeding by reason of Indemnitee's Corporate Status within thirty (30) days after the receipt by the Company of a statement or statements from Indemnitee requesting such advance or advances from time to time, whether prior to or after final disposition of such Proceeding. Such statement or statements shall reasonably evidence the Expenses incurred by Indemnitee and shall include or be preceded or accompanied by an undertaking by or on behalf of Indemnitee to repay any Expenses advanced if it shall ultimately be determined that Indemnitee is not entitled to be indemnified against such Expenses. Any advances and undertakings to repay pursuant to this Section 5 shall be unsecured and interest free.

6. Procedures and Presumptions for Determination of Entitlement to Indemnification. It is the intent of this Agreement to secure for Indemnitee rights of indemnity that are as favorable as may be permitted under the Delaware General Corporation Law and public policy of the State of Delaware. Accordingly, the parties agree that the following procedures and presumptions shall apply in the event of any question as to whether Indemnitee is entitled to indemnification under this Agreement:

(a) To obtain indemnification under this Agreement, Indemnitee shall submit to the Company a written request, including therein or therewith such documentation and information as is reasonably available to Indemnitee and is reasonably necessary to determine whether and to what extent Indemnitee is entitled to indemnification. The Secretary of the Company shall, promptly upon receipt of such a request for indemnification, advise the Board of Directors in writing that Indemnitee has requested indemnification.

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(b) Upon written request by Indemnitee for indemnification pursuant to the first sentence of Section 6(a) hereof, a determination, if required by applicable law, with respect to Indemnitee's entitlement thereto shall be made in the specific case by one of the following three methods, which shall be

at the election of the board: (1) by a majority vote of the disinterested directors, even though less than a quorum, by a committee of disinterested directors designated by a majority vote of the disinterested directors, even though less than a quorum, (2) if there are no disinterested directors or if the disinterested directors so direct, by independent legal counsel in a written opinion to the Board of Directors, a copy of which shall be delivered to the Indemnitee, or (3) if so directed by the Board of Directors, by the stockholders of the Company. For purposes hereof, disinterested directors are those members of the board of directors of the Company who are not parties to the action, suit or proceeding in respect of which indemnification is sought by Indemnitee.

(c) If the determination of entitlement to indemnification is to be made by Independent Counsel pursuant to Section 6(b) hereof, the Independent Counsel shall be selected as provided in this Section 6(c). The determination of whether Independent Counsel shall be engaged and the selection of such Independent Counsel shall be made by the Board of Directors. Indemnitee may, within 10 days after such written notice of selection shall have been given, deliver to the Company, as the case may be, a written objection to such selection; provided, however, that such objection may be asserted only on the ground that the Independent Counsel so selected does not meet the requirements of “**Independent Counsel**” as defined in Section 13 of this Agreement, and the objection shall set forth with particularity the factual basis of such assertion. Absent a proper and timely objection, the person so selected shall act as Independent Counsel. If a written objection is made and substantiated, the Independent Counsel selected may not serve as Independent Counsel unless and until such objection is withdrawn or a court has determined that such objection is without merit. If, within 20 days after submission by Indemnitee of a written request for indemnification pursuant to Section 6(a) hereof, no Independent Counsel shall have been selected and not objected to, either the Company or Indemnitee may petition the Court of Chancery of the State of Delaware or other court of competent jurisdiction for resolution of any objection which shall have been made by the Indemnitee to the Company’s selection of Independent Counsel and/or for the appointment as Independent Counsel of a person selected by the court or by such other person as the court shall designate, and the person with respect to whom all objections are so resolved or the person so appointed shall act as Independent Counsel under Section 6(b) hereof. The Company shall pay any and all reasonable fees and expenses of Independent Counsel incurred by such Independent Counsel in connection with acting pursuant to Section 6(b) hereof, and the Company shall pay all reasonable fees and expenses incident to the procedures of this Section 6(c), regardless of the manner in which such Independent Counsel was selected or appointed.

(d) In making a determination with respect to entitlement to indemnification hereunder, the person or persons or entity making such determination shall presume that Indemnitee is entitled to indemnification under this Agreement. Anyone seeking to overcome this presumption shall have the burden of proof and the burden of persuasion by clear and convincing evidence. Neither the failure of the Company (including by its directors or independent legal counsel) to have made a determination prior to the commencement of any action pursuant to this Agreement that indemnification is proper in the circumstances because Indemnitee has met the applicable standard of conduct, nor an actual determination by the Company (including by its directors or independent legal counsel) that Indemnitee has not met

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such applicable standard of conduct, shall be a defense to the action or create a presumption that Indemnitee has not met the applicable standard of conduct.

(e) Indemnitee shall be deemed to have acted in good faith if Indemnitee’s action is based on the records or books of account of the Enterprise (as hereinafter defined), including financial statements, or on information supplied to Indemnitee by the officers of the Enterprise in the course of their duties, or on the advice of legal counsel for the Enterprise or on information or records given or reports made to the Enterprise by an independent certified public accountant or by an appraiser or other expert selected with reasonable care by the Enterprise. In addition, the knowledge and/or actions, or failure to act, of any director, officer, agent or employee of the Enterprise shall not be imputed to Indemnitee for purposes of determining the right to indemnification under this Agreement. Whether or not the foregoing provisions of this Section 6(e) are satisfied, it shall in any event be presumed that Indemnitee has at all times acted in good faith and in a manner he reasonably believed to be in or not opposed to the best interests of the Company. Anyone seeking to overcome this presumption shall have the burden of proof and the burden of persuasion by clear and convincing evidence.

(f) If the person, persons or entity empowered or selected under Section 6 to determine whether Indemnitee is entitled to indemnification shall not have made a determination within sixty (60) days after receipt by the Company of the request therefor, the requisite determination of entitlement to indemnification shall be deemed to have been made and Indemnitee shall be entitled to such indemnification absent (i) a misstatement by Indemnitee of a material fact, or an omission of a material fact necessary to make Indemnitee’s statement not materially misleading, in connection with the request for indemnification, or (ii) a prohibition of such indemnification under applicable law; provided, however, that such 60-day period may be extended for a reasonable time, not to exceed an additional thirty (30) days, if the person, persons or entity making such determination with respect to entitlement to indemnification in good faith requires such additional time to obtain or evaluate documentation and/or information relating thereto; and provided, further, that the foregoing provisions of this Section 6(f) shall not apply if the determination of entitlement to indemnification is to be made by the stockholders pursuant to Section 6(b) of this Agreement and if (A) within fifteen (15) days after receipt by the Company of the request for such determination, the Board of Directors or the Disinterested Directors, if appropriate, resolve to submit such determination to the stockholders for their consideration at an annual meeting thereof to be held within seventy-five (75) days after such receipt and such determination is made thereat, or (B) a special meeting of stockholders is called within fifteen (15) days after such receipt for the purpose of making such determination, such meeting is held for such purpose within sixty (60) days after having been so called and such determination is made thereat.

(g) Indemnitee shall cooperate with the person, persons or entity making such determination with respect to Indemnitee’s entitlement to indemnification, including providing to such person, persons or entity upon reasonable advance request any documentation or information which is not privileged or otherwise protected from disclosure and which is reasonably available to Indemnitee and reasonably necessary to such determination. Any Independent Counsel, member of the Board of Directors or stockholder of the Company shall act reasonably and in good faith in making a determination regarding the Indemnitee’s entitlement to indemnification under this Agreement. Any costs or expenses (including attorneys’ fees and disbursements) incurred by Indemnitee in so cooperating with the person, persons or entity making such determination shall be borne by the Company (irrespective of the

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determination as to Indemnitee’s entitlement to indemnification) and the Company hereby indemnifies and agrees to hold Indemnitee harmless therefrom.

(h) The Company acknowledges that a settlement or other disposition short of final judgment may be successful if it permits a party to avoid expense, delay, distraction, disruption and uncertainty. In the event that any action, claim or proceeding to which Indemnitee is a party is resolved in any manner other than by adverse judgment against Indemnitee (including, without limitation, settlement of such action, claim or proceeding with or without payment of money or other consideration) it shall be presumed that Indemnitee has been successful on the merits or otherwise in such action, suit or proceeding. Anyone seeking to overcome this presumption shall have the burden of proof and the burden of persuasion by clear and convincing evidence.

(i) The termination of any Proceeding or of any claim, issue or matter therein, by judgment, order, settlement or conviction, or upon a plea of nolo contendere or its equivalent, shall not (except as otherwise expressly provided in this Agreement) of itself adversely affect the right of Indemnitee to

indemnification or create a presumption that Indemnitee did not act in good faith and in a manner which he reasonably believed to be in or not opposed to the best interests of the Company or, with respect to any criminal Proceeding, that Indemnitee had reasonable cause to believe that his conduct was unlawful.

7. Remedies of Indemnitee.

(a) In the event that (i) a determination is made pursuant to Section 6 of this Agreement that Indemnitee is not entitled to indemnification under this Agreement, (ii) advancement of Expenses is not timely made pursuant to Section 5 of this Agreement, (iii) no determination of entitlement to indemnification is made pursuant to Section 6(b) of this Agreement within 90 days after receipt by the Company of the request for indemnification, (iv) payment of indemnification is not made pursuant to this Agreement within ten (10) days after receipt by the Company of a written request therefor or (v) payment of indemnification is not made within ten (10) days after a determination has been made that Indemnitee is entitled to indemnification or such determination is deemed to have been made pursuant to Section 6 of this Agreement, Indemnitee shall be entitled to an adjudication in an appropriate court of the State of Delaware, or in any other court of competent jurisdiction, of Indemnitee's entitlement to such indemnification. Indemnitee shall commence such proceeding seeking an adjudication within 180 days following the date on which Indemnitee first has the right to commence such proceeding pursuant to this Section 7(a). The Company shall not oppose Indemnitee's right to seek any such adjudication.

(b) In the event that a determination shall have been made pursuant to Section 6(b) of this Agreement that Indemnitee is not entitled to indemnification, any judicial proceeding commenced pursuant to this Section 7 shall be conducted in all respects as a de novo trial on the merits, and Indemnitee shall not be prejudiced by reason of the adverse determination under Section 6(b).

(c) If a determination shall have been made pursuant to Section 6(b) of this Agreement that Indemnitee is entitled to indemnification, the Company shall be bound by such determination in any judicial proceeding commenced pursuant to this Section 7, absent (i) a misstatement by Indemnitee of a material fact, or an omission of a material fact necessary to

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make Indemnitee's statement not materially misleading in connection with the application for indemnification, or (ii) a prohibition of such indemnification under applicable law.

(d) In the event that Indemnitee, pursuant to this Section 7, seeks a judicial adjudication of his rights under, or to recover damages for breach of, this Agreement, or to recover under any directors' and officers' liability insurance policies maintained by the Company, the Company shall pay on his behalf, in advance, any and all expenses (of the types described in the definition of Expenses in Section 13 of this Agreement) actually and reasonably incurred by him in such judicial adjudication, regardless of whether Indemnitee ultimately is determined to be entitled to such indemnification, advancement of expenses or insurance recovery.

(e) The Company shall be precluded from asserting in any judicial proceeding commenced pursuant to this Section 7 that the procedures and presumptions of this Agreement are not valid, binding and enforceable and shall stipulate in any such court that the Company is bound by all the provisions of this Agreement. The Company shall indemnify Indemnitee against any and all Expenses and, if requested by Indemnitee, shall (within ten (10) days after receipt by the Company of a written request therefore) advance, to the extent not prohibited by law, such expenses to Indemnitee, which are incurred by Indemnitee in connection with any action brought by Indemnitee for indemnification or advance of Expenses from the Company under this Agreement or under any directors' and officers' liability insurance policies maintained by the Company, regardless of whether Indemnitee ultimately is determined to be entitled to such indemnification, advancement of Expenses or insurance recovery, as the case may be.

(f) Notwithstanding anything in this Agreement to the contrary, no determination as to entitlement to indemnification under this Agreement shall be required to be made prior to the final disposition of the Proceeding.

8. Non-Exclusivity; Survival of Rights; Insurance; Subrogation.

(a) The rights of indemnification as provided by this Agreement shall not be deemed exclusive of any other rights to which Indemnitee may at any time be entitled under applicable law, the certificate of incorporation of the Company, the Bylaws, any agreement, a vote of stockholders, a resolution of directors or otherwise. No amendment, alteration or repeal of this Agreement or of any provision hereof shall limit or restrict any right of Indemnitee under this Agreement in respect of any action taken or omitted by such Indemnitee in his Corporate Status prior to such amendment, alteration or repeal. To the extent that a change in the Delaware General Corporation Law, whether by statute or judicial decision, permits greater indemnification than would be afforded currently under the Bylaws and this Agreement, it is the intent of the parties hereto that Indemnitee shall enjoy by this Agreement the greater benefits so afforded by such change. No right or remedy herein conferred is intended to be exclusive of any other right or remedy, and every other right and remedy shall be cumulative and in addition to every other right and remedy given hereunder or now or hereafter existing at law or in equity or otherwise. The assertion or employment of any right or remedy hereunder, or otherwise, shall not prevent the concurrent assertion or employment of any other right or remedy.

(b) To the extent that the Company maintains an insurance policy or policies providing liability insurance for directors, officers, employees, or agents or fiduciaries of

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the Company or of any other corporation, partnership, joint venture, trust, employee benefit plan or other enterprise that such person serves at the request of the Company, Indemnitee shall be covered by such policy or policies in accordance with its or their terms to the maximum extent of the coverage available for any director, officer, employee, agent or fiduciary under such policy or policies. If, at the time of the receipt of a notice of a claim pursuant to the terms hereof, the Company has director and officer liability insurance in effect, the Company shall give prompt notice of the commencement of such proceeding to the insurers in accordance with the procedures set forth in the respective policies. The Company shall thereafter take all necessary or desirable action to cause such insurers to pay, on behalf of the Indemnitee, all amounts payable as a result of such proceeding in accordance with the terms of such policies.

(c) In the event of any payment under this Agreement, the Company shall be subrogated to the extent of such payment to all of the rights of recovery of Indemnitee, who shall execute all papers required and take all action necessary to secure such rights, including execution of such documents as are necessary to enable the Company to bring suit to enforce such rights.

(d) The Company shall not be liable under this Agreement to make any payment of amounts otherwise indemnifiable hereunder if and to the extent that Indemnitee has otherwise actually received such payment under any insurance policy, contract, agreement or otherwise.

(e) The Company's obligation to indemnify or advance Expenses hereunder to Indemnitee who is or was serving at the request of the Company as a director, officer, employee or agent of any other corporation, partnership, joint venture, trust, employee benefit plan or other enterprise shall be reduced by any amount Indemnitee has actually received as indemnification or advancement of expenses from such other corporation, partnership, joint venture, trust, employee benefit plan or other enterprise.

9. Exception to Right of Indemnification. Notwithstanding any provision in this Agreement, the Company shall not be obligated under this Agreement to make any indemnity in connection with any claim made against Indemnitee:

(a) for which payment has actually been made to or on behalf of Indemnitee under any insurance policy or other indemnity provision, except with respect to any excess beyond the amount paid under any insurance policy or other indemnity provision; or

(b) for an accounting of profits made from the purchase and sale (or sale and purchase) by Indemnitee of securities of the Company within the meaning of Section 16(b) of the Securities Exchange Act of 1934, as amended, or similar provisions of state statutory law or common law; or

(c) in connection with any Proceeding (or any part of any Proceeding) initiated by Indemnitee, including any Proceeding (or any part of any Proceeding) initiated by Indemnitee against the Company or its directors, officers, employees or other indemnitees, unless (i) the Board of Directors of the Company authorized the Proceeding (or any part of any Proceeding) prior to its initiation or (ii) the Company provides the indemnification, in its sole discretion, pursuant to the powers vested in the Company under applicable law.

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10. Duration of Agreement. All agreements and obligations of the Company contained herein shall continue during the period Indemnitee is a director of the Company (or is or was serving at the request of the Company as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise) and for a period of five (5) years thereafter, and in addition shall continue thereafter so long as Indemnitee shall be subject to any Proceeding (or any proceeding commenced under Section 7 hereof) by reason of his Corporate Status, whether or not he is acting or serving in any such capacity at the time any liability or expense is incurred for which indemnification can be provided under this Agreement. This Agreement shall be binding upon and inure to the benefit of and be enforceable by the parties hereto and their respective successors (including any direct or indirect successor by purchase, merger, consolidation or otherwise to all or substantially all of the business or assets of the Company), assigns, spouses, heirs, executors and personal and legal representatives.

11. Security. To the extent requested by Indemnitee and approved by the Board of Directors of the Company, the Company may at any time and from time to time provide security to Indemnitee for the Company's obligations hereunder through an irrevocable bank line of credit, funded trust or other collateral. Any such security, once provided to Indemnitee, may not be revoked or released without the prior written consent of the Indemnitee.

12. Enforcement.

(a) The Company expressly confirms and agrees that it has entered into this Agreement and assumes the obligations imposed on it hereby in order to induce Indemnitee to serve as a director of the Company, and the Company acknowledges that Indemnitee is relying upon this Agreement in serving as a director of the Company.

(b) This Agreement constitutes the entire agreement between the parties hereto with respect to the subject matter hereof and supersedes all prior agreements and understandings, oral, written and implied, between the parties hereto with respect to the subject matter hereof.

13. Definitions. For purposes of this Agreement:

(a) "**Corporate Status**" describes the status of a person who is or was a director, officer, employee, agent or fiduciary of the Company or of any other corporation, partnership, joint venture, trust, employee benefit plan or other enterprise that such person is or was serving at the express written request of the Company.

(b) "**Disinterested Director**" means a director of the Company who is not and was not a party to the Proceeding in respect of which indemnification is sought by Indemnitee.

(c) "**Enterprise**" shall mean the Company and any other corporation, partnership, joint venture, trust, employee benefit plan or other enterprise that Indemnitee is or was serving at the express written request of the Company as a director, officer, employee, agent or fiduciary.

(d) "**Expenses**" shall include all reasonable attorneys' fees, retainers, court costs, transcript costs, fees of experts, witness fees, travel expenses, duplicating costs,

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printing and binding costs, telephone charges, postage, delivery service fees and all other disbursements or expenses of the types customarily incurred in connection with prosecuting, defending, preparing to prosecute or defend, investigating, participating, or being or preparing to be a witness in a Proceeding. Expenses also shall include Expenses incurred in connection with any appeal resulting from any Proceeding, including without limitation the premium, security for, and other costs relating to any cost bond, supersedeas bond, or other appeal bond or its equivalent. Expenses, however, shall not include amounts paid in settlement by Indemnitee or the amount of judgments or fines against Indemnitee.

(e) "**Independent Counsel**" means a law firm, or a member of a law firm, that is experienced in matters of corporation law and neither presently is, nor in the past five years has been, retained to represent: (i) the Company or Indemnitee in any matter material to either such party (other than with respect to matters concerning Indemnitee under this Agreement, or of other indemnitees under similar indemnification agreements), or (ii) any other party to the Proceeding giving rise to a claim for indemnification hereunder. Notwithstanding the foregoing, the term "Independent Counsel" shall not include any person who, under the applicable standards of professional conduct then prevailing, would have a conflict of interest in representing either the Company or Indemnitee in an action to determine Indemnitee's rights under this Agreement. The Company agrees to pay the reasonable fees of the Independent Counsel referred to above and to fully indemnify such counsel against any and all Expenses, claims, liabilities and damages arising out of or relating to this Agreement or its engagement pursuant hereto.

(f) **“Proceeding”** includes any threatened, pending or completed action, suit, arbitration, alternate dispute resolution mechanism, investigation, inquiry, administrative hearing or any other actual, threatened or completed proceeding, whether brought by or in the right of the Company or otherwise and whether civil, criminal, administrative or investigative, in which Indemnitee was, is or will be involved as a party or otherwise, by reason of the fact that Indemnitee is or was a director of the Company, by reason of any action taken by him or of any inaction on his part while acting as a director of the Company, or by reason of the fact that he is or was serving at the request of the Company as a director, officer, employee, agent or fiduciary of another corporation, partnership, joint venture, trust or other Enterprise; in each case whether or not he is acting or serving in any such capacity at the time any liability or expense is incurred for which indemnification can be provided under this Agreement; including one pending on or before the date of this Agreement, but excluding one initiated by an Indemnitee pursuant to Section 7 of this Agreement to enforce his rights under this Agreement.

14. **Severability.** The invalidity or unenforceability of any provision hereof shall in no way affect the validity or enforceability of any other provision. Without limiting the generality of the foregoing, this Agreement is intended to confer upon Indemnitee indemnification rights to the fullest extent permitted by applicable laws. In the event any provision hereof conflicts with any applicable law, such provision shall be deemed modified, consistent with the aforementioned intent, to the extent necessary to resolve such conflict.

15. **Modification and Waiver.** No supplement, modification, termination or amendment of this Agreement shall be binding unless executed in writing by both of the parties hereto. No waiver of any of the provisions of this Agreement shall be deemed or shall constitute a waiver of any other provisions hereof (whether or not similar) nor shall such waiver constitute a continuing waiver.

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16. **Notice By Indemnitee.** Indemnitee agrees promptly to notify the Company in writing upon being served with or otherwise receiving any summons, citation, subpoena, complaint, indictment, information or other document relating to any Proceeding or matter which may be subject to indemnification covered hereunder. The failure to so notify the Company shall not relieve the Company of any obligation which it may have to Indemnitee under this Agreement or otherwise unless and only to the extent that such failure or delay materially prejudices the Company.

17. **Notices.** All notices and other communications given or made pursuant to this Agreement shall be in writing and shall be deemed effectively given: (a) upon personal delivery to the party to be notified, (b) when sent by confirmed electronic mail or facsimile if sent during normal business hours of the recipient, and if not so confirmed, then on the next business day, (c) five (5) days after having been sent by registered or certified mail, return receipt requested, postage prepaid, or (d) one (1) day after deposit with a nationally recognized overnight courier, specifying next day delivery, with written verification of receipt. All communications shall be sent:

(a) To Indemnitee at the address set forth below Indemnitee’s signature hereto.

(b) To the Company at:

200 West Street  
Waltham, MA 02451  
Attention: CEO

or to such other address as may have been furnished to Indemnitee by the Company or to the Company by Indemnitee, as the case may be.

18. **Counterparts.** This Agreement may be executed in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same Agreement. This Agreement may also be executed and delivered by facsimile signature and in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument.

19. **Headings.** The headings of the paragraphs of this Agreement are inserted for convenience only and shall not be deemed to constitute part of this Agreement or to affect the construction thereof.

20. **Governing Law and Consent to Jurisdiction.** This Agreement and the legal relations among the parties shall be governed by, and construed and enforced in accordance with, the laws of the State of Delaware, without regard to its conflict of laws rules. The Company and Indemnitee hereby irrevocably and unconditionally (i) agree that any action or proceeding arising out of or in connection with this Agreement shall be brought only in the Chancery Court of the State of Delaware (the **“Delaware Court”**), and not in any other state or federal court in the United States of America or any court in any other country, (ii) consent to submit to the exclusive jurisdiction of the Delaware Court for purposes of any action or proceeding arising out of or in connection with this Agreement, (iii) waive any objection to the laying of venue of any such action or proceeding in the Delaware Court, and (iv) waive, and agree not to plead or to

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make, any claim that any such action or proceeding brought in the Delaware Court has been brought in an improper or inconvenient forum.

**SIGNATURE PAGE TO FOLLOW**

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IN WITNESS WHEREOF, the parties hereto have executed this Indemnification Agreement on and as of the day and year first above written.

**PROTEON THERAPEUTICS, INC.**

By: /s/ Steve Burke  
Name: Steve Burke  
Title: Chief Medical Officer



**INDEMNITEE**

/s/ Timothy Noyes

Name: Timothy P. Noyes

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Address:

Proteon Therapeutics

200 West Street

Waltham, MA 02451

**SIGNATURE PAGE TO INDEMNIFICATION AGREEMENT - NOYES**

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## INDEMNIFICATION AGREEMENT

## INDEMNIFICATION AGREEMENT

THIS INDEMNIFICATION AGREEMENT (the "**Agreement**") is made and entered into as of May 13, 2014 between **PROTEON THERAPEUTICS, INC.**, a Delaware corporation (the "**Company**"), and Tim Haines ("**Indemnitee**").

WITNESSETH THAT:

WHEREAS, highly competent persons have become more reluctant to serve corporations as directors or in other capacities unless they are provided with adequate protection through insurance or adequate indemnification against inordinate risks of claims and actions against them arising out of their service to and activities on behalf of the corporation;

WHEREAS, the Board of Directors of the Company (the "**Board**") has determined that, in order to attract and retain qualified individuals, the Company will attempt to maintain on an ongoing basis, at its sole expense, liability insurance to protect persons serving the Company and its subsidiaries from certain liabilities. Although the furnishing of such insurance has been a customary and widespread practice among United States-based corporations and other business enterprises, the Company believes that, given current market conditions and trends, such insurance may be available to it in the future only at higher premiums and with more exclusions. At the same time, directors, officers, and other persons in service to corporations or business enterprises are being increasingly subjected to expensive and time-consuming litigation relating to, among other things, matters that traditionally would have been brought only against the Company or business enterprise itself. The Certificate of Incorporation of the Company permits, and the By-laws of the Company require, indemnification of directors of the Company. Indemnitee may also be entitled to indemnification pursuant to the General Corporation Law of the State of Delaware ("**DGCL**"). The By-laws and the DGCL expressly provide that the indemnification provisions set forth therein are not exclusive, and thereby contemplate that contracts may be entered into between the Company and members of the board of directors with respect to indemnification;

WHEREAS, the uncertainties relating to such insurance and to indemnification have increased the difficulty of attracting and retaining such persons;

WHEREAS, the Board has determined that the increased difficulty in attracting and retaining such persons is detrimental to the best interests of the Company's stockholders and that the Company should act to assure such persons that there will be increased certainty of such protection in the future;

WHEREAS, it is reasonable, prudent and necessary for the Company contractually to obligate itself to indemnify, and to advance expenses on behalf of, such persons to the fullest extent permitted by applicable law so that they will serve or continue to serve the Company free from undue concern that they will not be so indemnified;

WHEREAS, this Agreement is a supplement to and in furtherance of the By-laws of the Company and any resolutions adopted pursuant thereto, and shall not be deemed a substitute therefor, nor to diminish or abrogate any rights of Indemnitee thereunder;

WHEREAS, Indemnitee does not regard the protection available under the Company's By-laws and insurance as adequate in the present circumstances, and may not be willing to serve as a director without adequate protection, and the Company desires Indemnitee to serve in such capacity. Indemnitee is willing to serve, continue to serve and to take on additional service for or on behalf of the Company on the condition that he be so indemnified; and

NOW, THEREFORE, in consideration of Indemnitee's agreement to serve as a director after the date hereof, the parties hereto agree as follows:

1. Indemnity of Indemnitee. The Company hereby agrees to hold harmless and indemnify Indemnitee to the fullest extent permitted by law, as such may be amended from time to time. In furtherance of the foregoing indemnification, and without limiting the generality thereof:

(a) Proceedings Other Than Proceedings by or in the Right of the Company. Indemnitee shall be entitled to the rights of indemnification provided in this Section 1(a) if, by reason of his Corporate Status (as hereinafter defined), the Indemnitee is, or is threatened to be made, a party to or participant in any Proceeding (as hereinafter defined) other than a Proceeding by or in the right of the Company. Pursuant to this Section 1(a), Indemnitee shall be indemnified against all Expenses (as hereinafter defined), judgments, penalties, fines and amounts paid in settlement actually and reasonably incurred by him, or on his behalf, in connection with such Proceeding or any claim, issue or matter therein, if the Indemnitee acted in good faith and in a manner the Indemnitee reasonably believed to be in or not opposed to the best interests of the Company, and with respect to any criminal Proceeding, had no reasonable cause to believe the Indemnitee's conduct was unlawful.

(b) Proceedings by or in the Right of the Company. Indemnitee shall be entitled to the rights of indemnification provided in this Section 1(b) if, by reason of his Corporate Status, the Indemnitee is, or is threatened to be made, a party to or participant in any Proceeding brought by or in the right of the Company. Pursuant to this Section 1(b), Indemnitee shall be indemnified against all Expenses actually and reasonably incurred by the Indemnitee, or on the Indemnitee's behalf, in connection with such Proceeding if the Indemnitee acted in good faith and in a manner the Indemnitee reasonably believed to be in or not opposed to the best interests of the Company; provided, however, if applicable law so provides, no indemnification against such Expenses shall be made in respect of any claim, issue or matter in such Proceeding as to which Indemnitee shall have been adjudged to be liable to the Company unless and to the extent that the Court of Chancery of the State of Delaware shall determine that such indemnification may be made.

(c) Indemnification for Expenses of a Party Who is Wholly or Partly Successful. Notwithstanding any other provision of this Agreement, to the extent that Indemnitee is, by reason of his Corporate Status, a party to and is successful, on the merits or otherwise, in any Proceeding, he shall be indemnified to the maximum extent permitted by law, as such may be amended from time to time, against all Expenses actually and reasonably incurred by him or on his behalf in connection therewith. If Indemnitee is not wholly successful in such Proceeding but is successful, on the merits or otherwise, as to one or more but less than all claims, issues or matters in such Proceeding, the Company shall indemnify Indemnitee against all Expenses actually and reasonably incurred by him or on his behalf in connection with each successfully resolved claim, issue or matter. For purposes of this Section and without

limitation, the termination of any claim, issue or matter in such a Proceeding by dismissal, with or without prejudice, shall be deemed to be a successful result as to such claim, issue or matter.

2. Additional Indemnity. In addition to, and without regard to any limitations on, the indemnification provided for in Section 1 of this Agreement, the Company shall and hereby does indemnify and hold harmless Indemnitee against all Expenses, judgments, penalties, fines and amounts paid in settlement actually and reasonably incurred by him or on his behalf if, by reason of his Corporate Status, he is, or is threatened to be made, a party to or participant in any Proceeding (including a Proceeding by or in the right of the Company), including, without limitation, all liability arising out of the negligence or active or passive wrongdoing of Indemnitee. The only limitation that shall exist upon the Company's obligations pursuant to this Agreement shall be that the Company shall not be obligated to make any payment to Indemnitee that is finally determined (under the procedures, and subject to the presumptions, set forth in Sections 6 and 7 hereof) to be unlawful.

3. Contribution.

(a) Whether or not the indemnification provided in Sections 1 and 2 hereof is available, in respect of any threatened, pending or completed action, suit or proceeding in which the Company is jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding), the Company shall pay, in the first instance, the entire amount of any judgment or settlement of such action, suit or proceeding without requiring Indemnitee to contribute to such payment and the Company hereby waives and relinquishes any right of contribution it may have against Indemnitee. The Company shall not enter into any settlement of any action, suit or proceeding in which the Company is jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding) unless such settlement provides for a full and final release of all claims asserted against Indemnitee.

(b) Without diminishing or impairing the obligations of the Company set forth in the preceding subparagraph, if, for any reason, Indemnitee shall elect or be required to pay all or any portion of any judgment or settlement in any threatened, pending or completed action, suit or proceeding in which the Company is jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding), the Company shall contribute to the amount of expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred and paid or payable by Indemnitee in proportion to the relative benefits received by the Company and all officers, directors or employees of the Company, other than Indemnitee, who are jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding), on the one hand, and Indemnitee, on the other hand, from the transaction from which such action, suit or proceeding arose; provided, however, that the proportion determined on the basis of relative benefit may, to the extent necessary to conform to law, be further adjusted by reference to the relative fault of the Company and all officers, directors or employees of the Company other than Indemnitee who are jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding), on the one hand, and Indemnitee, on the other hand, in connection with the events that resulted in such expenses, judgments, fines or settlement amounts, as well as any other equitable considerations which the Law may require to be considered. The relative fault of the Company and all officers, directors or employees of the Company, other than Indemnitee, who are jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding), on the one hand, and Indemnitee, on the other hand, shall be determined by reference to, among other things, the degree to which their actions were motivated

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by intent to gain personal profit or advantage, the degree to which their liability is primary or secondary and the degree to which their conduct is active or passive.

(c) The Company hereby agrees to fully indemnify and hold Indemnitee harmless from any claims of contribution which may be brought by officers, directors or employees of the Company, other than Indemnitee, who may be jointly liable with Indemnitee.

(d) To the fullest extent permissible under applicable law, if the indemnification provided for in this Agreement is unavailable to Indemnitee for any reason whatsoever, the Company, in lieu of indemnifying Indemnitee, shall contribute to the amount incurred by Indemnitee, whether for judgments, fines, penalties, excise taxes, amounts paid or to be paid in settlement and/or for Expenses, in connection with any claim relating to an indemnifiable event under this Agreement, in such proportion as is deemed fair and reasonable in light of all of the circumstances of such Proceeding in order to reflect (i) the relative benefits received by the Company and Indemnitee as a result of the event(s) and/or transaction(s) giving cause to such Proceeding; and/or (ii) the relative fault of the Company (and its directors, officers, employees and agents) and Indemnitee in connection with such event(s) and/or transaction(s).

4. Indemnification for Expenses of a Witness. Notwithstanding any other provision of this Agreement, to the extent that Indemnitee is, by reason of his Corporate Status, a witness in any Proceeding to which Indemnitee is not a party, he shall be indemnified against all Expenses actually and reasonably incurred by him or on his behalf in connection therewith.

5. Advancement of Expenses. Notwithstanding any other provision of this Agreement, the Company shall advance all Expenses incurred by or on behalf of Indemnitee in connection with any Proceeding by reason of Indemnitee's Corporate Status within thirty (30) days after the receipt by the Company of a statement or statements from Indemnitee requesting such advance or advances from time to time, whether prior to or after final disposition of such Proceeding. Such statement or statements shall reasonably evidence the Expenses incurred by Indemnitee and shall include or be preceded or accompanied by an undertaking by or on behalf of Indemnitee to repay any Expenses advanced if it shall ultimately be determined that Indemnitee is not entitled to be indemnified against such Expenses. Any advances and undertakings to repay pursuant to this Section 5 shall be unsecured and interest free.

6. Procedures and Presumptions for Determination of Entitlement to Indemnification. It is the intent of this Agreement to secure for Indemnitee rights of indemnity that are as favorable as may be permitted under the Delaware General Corporation Law and public policy of the State of Delaware. Accordingly, the parties agree that the following procedures and presumptions shall apply in the event of any question as to whether Indemnitee is entitled to indemnification under this Agreement:

(a) To obtain indemnification under this Agreement, Indemnitee shall submit to the Company a written request, including therein or therewith such documentation and information as is reasonably available to Indemnitee and is reasonably necessary to determine whether and to what extent Indemnitee is entitled to indemnification. The Secretary of the Company shall, promptly upon receipt of such a request for indemnification, advise the Board of Directors in writing that Indemnitee has requested indemnification.

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(b) Upon written request by Indemnitee for indemnification pursuant to the first sentence of Section 6(a) hereof, a determination, if required by applicable law, with respect to Indemnitee's entitlement thereto shall be made in the specific case by one of the following three methods, which shall be

at the election of the board: (1) by a majority vote of the disinterested directors, even though less than a quorum, by a committee of disinterested directors designated by a majority vote of the disinterested directors, even though less than a quorum, (2) if there are no disinterested directors or if the disinterested directors so direct, by independent legal counsel in a written opinion to the Board of Directors, a copy of which shall be delivered to the Indemnitee, or (3) if so directed by the Board of Directors, by the stockholders of the Company. For purposes hereof, disinterested directors are those members of the board of directors of the Company who are not parties to the action, suit or proceeding in respect of which indemnification is sought by Indemnitee.

(c) If the determination of entitlement to indemnification is to be made by Independent Counsel pursuant to Section 6(b) hereof, the Independent Counsel shall be selected as provided in this Section 6(c). The determination of whether Independent Counsel shall be engaged and the selection of such Independent Counsel shall be made by the Board of Directors. Indemnitee may, within 10 days after such written notice of selection shall have been given, deliver to the Company, as the case may be, a written objection to such selection; provided, however, that such objection may be asserted only on the ground that the Independent Counsel so selected does not meet the requirements of “**Independent Counsel**” as defined in Section 13 of this Agreement, and the objection shall set forth with particularity the factual basis of such assertion. Absent a proper and timely objection, the person so selected shall act as Independent Counsel. If a written objection is made and substantiated, the Independent Counsel selected may not serve as Independent Counsel unless and until such objection is withdrawn or a court has determined that such objection is without merit. If, within 20 days after submission by Indemnitee of a written request for indemnification pursuant to Section 6(a) hereof, no Independent Counsel shall have been selected and not objected to, either the Company or Indemnitee may petition the Court of Chancery of the State of Delaware or other court of competent jurisdiction for resolution of any objection which shall have been made by the Indemnitee to the Company’s selection of Independent Counsel and/or for the appointment as Independent Counsel of a person selected by the court or by such other person as the court shall designate, and the person with respect to whom all objections are so resolved or the person so appointed shall act as Independent Counsel under Section 6(b) hereof. The Company shall pay any and all reasonable fees and expenses of Independent Counsel incurred by such Independent Counsel in connection with acting pursuant to Section 6(b) hereof, and the Company shall pay all reasonable fees and expenses incident to the procedures of this Section 6(c), regardless of the manner in which such Independent Counsel was selected or appointed.

(d) In making a determination with respect to entitlement to indemnification hereunder, the person or persons or entity making such determination shall presume that Indemnitee is entitled to indemnification under this Agreement. Anyone seeking to overcome this presumption shall have the burden of proof and the burden of persuasion by clear and convincing evidence. Neither the failure of the Company (including by its directors or independent legal counsel) to have made a determination prior to the commencement of any action pursuant to this Agreement that indemnification is proper in the circumstances because Indemnitee has met the applicable standard of conduct, nor an actual determination by the Company (including by its directors or independent legal counsel) that Indemnitee has not met

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such applicable standard of conduct, shall be a defense to the action or create a presumption that Indemnitee has not met the applicable standard of conduct.

(e) Indemnitee shall be deemed to have acted in good faith if Indemnitee’s action is based on the records or books of account of the Enterprise (as hereinafter defined), including financial statements, or on information supplied to Indemnitee by the officers of the Enterprise in the course of their duties, or on the advice of legal counsel for the Enterprise or on information or records given or reports made to the Enterprise by an independent certified public accountant or by an appraiser or other expert selected with reasonable care by the Enterprise. In addition, the knowledge and/or actions, or failure to act, of any director, officer, agent or employee of the Enterprise shall not be imputed to Indemnitee for purposes of determining the right to indemnification under this Agreement. Whether or not the foregoing provisions of this Section 6(e) are satisfied, it shall in any event be presumed that Indemnitee has at all times acted in good faith and in a manner he reasonably believed to be in or not opposed to the best interests of the Company. Anyone seeking to overcome this presumption shall have the burden of proof and the burden of persuasion by clear and convincing evidence.

(f) If the person, persons or entity empowered or selected under Section 6 to determine whether Indemnitee is entitled to indemnification shall not have made a determination within sixty (60) days after receipt by the Company of the request therefor, the requisite determination of entitlement to indemnification shall be deemed to have been made and Indemnitee shall be entitled to such indemnification absent (i) a misstatement by Indemnitee of a material fact, or an omission of a material fact necessary to make Indemnitee’s statement not materially misleading, in connection with the request for indemnification, or (ii) a prohibition of such indemnification under applicable law; provided, however, that such 60-day period may be extended for a reasonable time, not to exceed an additional thirty (30) days, if the person, persons or entity making such determination with respect to entitlement to indemnification in good faith requires such additional time to obtain or evaluate documentation and/or information relating thereto; and provided, further, that the foregoing provisions of this Section 6(f) shall not apply if the determination of entitlement to indemnification is to be made by the stockholders pursuant to Section 6(b) of this Agreement and if (A) within fifteen (15) days after receipt by the Company of the request for such determination, the Board of Directors or the Disinterested Directors, if appropriate, resolve to submit such determination to the stockholders for their consideration at an annual meeting thereof to be held within seventy-five (75) days after such receipt and such determination is made thereat, or (B) a special meeting of stockholders is called within fifteen (15) days after such receipt for the purpose of making such determination, such meeting is held for such purpose within sixty (60) days after having been so called and such determination is made thereat.

(g) Indemnitee shall cooperate with the person, persons or entity making such determination with respect to Indemnitee’s entitlement to indemnification, including providing to such person, persons or entity upon reasonable advance request any documentation or information which is not privileged or otherwise protected from disclosure and which is reasonably available to Indemnitee and reasonably necessary to such determination. Any Independent Counsel, member of the Board of Directors or stockholder of the Company shall act reasonably and in good faith in making a determination regarding the Indemnitee’s entitlement to indemnification under this Agreement. Any costs or expenses (including attorneys’ fees and disbursements) incurred by Indemnitee in so cooperating with the person,

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persons or entity making such determination shall be borne by the Company (irrespective of the determination as to Indemnitee’s entitlement to indemnification) and the Company hereby indemnifies and agrees to hold Indemnitee harmless therefrom.

(h) The Company acknowledges that a settlement or other disposition short of final judgment may be successful if it permits a party to avoid expense, delay, distraction, disruption and uncertainty. In the event that any action, claim or proceeding to which Indemnitee is a party is resolved in any manner other than by adverse judgment against Indemnitee (including, without limitation, settlement of such action, claim or proceeding with or without payment of money or other consideration) it shall be presumed that Indemnitee has been successful on the merits or otherwise in such action, suit or proceeding. Anyone seeking to overcome this presumption shall have the burden of proof and the burden of persuasion by clear and convincing evidence.

(i) The termination of any Proceeding or of any claim, issue or matter therein, by judgment, order, settlement or conviction, or upon a plea of nolo contendere or its equivalent, shall not (except as otherwise expressly provided in this Agreement) of itself adversely affect the right of Indemnitee to

indemnification or create a presumption that Indemnitee did not act in good faith and in a manner which he reasonably believed to be in or not opposed to the best interests of the Company or, with respect to any criminal Proceeding, that Indemnitee had reasonable cause to believe that his conduct was unlawful.

7. Remedies of Indemnitee.

(a) In the event that (i) a determination is made pursuant to Section 6 of this Agreement that Indemnitee is not entitled to indemnification under this Agreement, (ii) advancement of Expenses is not timely made pursuant to Section 5 of this Agreement, (iii) no determination of entitlement to indemnification is made pursuant to Section 6(b) of this Agreement within 90 days after receipt by the Company of the request for indemnification, (iv) payment of indemnification is not made pursuant to this Agreement within ten (10) days after receipt by the Company of a written request therefor or (v) payment of indemnification is not made within ten (10) days after a determination has been made that Indemnitee is entitled to indemnification or such determination is deemed to have been made pursuant to Section 6 of this Agreement, Indemnitee shall be entitled to an adjudication in an appropriate court of the State of Delaware, or in any other court of competent jurisdiction, of Indemnitee's entitlement to such indemnification. Indemnitee shall commence such proceeding seeking an adjudication within 180 days following the date on which Indemnitee first has the right to commence such proceeding pursuant to this Section 7(a). The Company shall not oppose Indemnitee's right to seek any such adjudication.

(b) In the event that a determination shall have been made pursuant to Section 6(b) of this Agreement that Indemnitee is not entitled to indemnification, any judicial proceeding commenced pursuant to this Section 7 shall be conducted in all respects as a de novo trial on the merits, and Indemnitee shall not be prejudiced by reason of the adverse determination under Section 6(b).

(c) If a determination shall have been made pursuant to Section 6(b) of this Agreement that Indemnitee is entitled to indemnification, the Company shall be bound by such determination in any judicial proceeding commenced pursuant to this Section 7, absent (i) a

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misstatement by Indemnitee of a material fact, or an omission of a material fact necessary to make Indemnitee's statement not materially misleading in connection with the application for indemnification, or (ii) a prohibition of such indemnification under applicable law.

(d) In the event that Indemnitee, pursuant to this Section 7, seeks a judicial adjudication of his rights under, or to recover damages for breach of, this Agreement, or to recover under any directors' and officers' liability insurance policies maintained by the Company, the Company shall pay on his behalf, in advance, any and all expenses (of the types described in the definition of Expenses in Section 13 of this Agreement) actually and reasonably incurred by him in such judicial adjudication, regardless of whether Indemnitee ultimately is determined to be entitled to such indemnification, advancement of expenses or insurance recovery.

(e) The Company shall be precluded from asserting in any judicial proceeding commenced pursuant to this Section 7 that the procedures and presumptions of this Agreement are not valid, binding and enforceable and shall stipulate in any such court that the Company is bound by all the provisions of this Agreement. The Company shall indemnify Indemnitee against any and all Expenses and, if requested by Indemnitee, shall (within ten (10) days after receipt by the Company of a written request therefore) advance, to the extent not prohibited by law, such expenses to Indemnitee, which are incurred by Indemnitee in connection with any action brought by Indemnitee for indemnification or advance of Expenses from the Company under this Agreement or under any directors' and officers' liability insurance policies maintained by the Company, regardless of whether Indemnitee ultimately is determined to be entitled to such indemnification, advancement of Expenses or insurance recovery, as the case may be.

(f) Notwithstanding anything in this Agreement to the contrary, no determination as to entitlement to indemnification under this Agreement shall be required to be made prior to the final disposition of the Proceeding.

8. Non-Exclusivity; Survival of Rights; Insurance; Primacy of Indemnification; Subrogation.

(a) The rights of indemnification as provided by this Agreement shall not be deemed exclusive of any other rights to which Indemnitee may at any time be entitled under applicable law, the certificate of incorporation of the Company, the Bylaws, any agreement, a vote of stockholders, a resolution of directors or otherwise. No amendment, alteration or repeal of this Agreement or of any provision hereof shall limit or restrict any right of Indemnitee under this Agreement in respect of any action taken or omitted by such Indemnitee in his Corporate Status prior to such amendment, alteration or repeal. To the extent that a change in the Delaware General Corporation Law, whether by statute or judicial decision, permits greater indemnification than would be afforded currently under the Bylaws and this Agreement, it is the intent of the parties hereto that Indemnitee shall enjoy by this Agreement the greater benefits so afforded by such change. No right or remedy herein conferred is intended to be exclusive of any other right or remedy, and every other right and remedy shall be cumulative and in addition to every other right and remedy given hereunder or now or hereafter existing at law or in equity or otherwise. The assertion or employment of any right or remedy hereunder, or otherwise, shall not prevent the concurrent assertion or employment of any other right or remedy.

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(b) To the extent that the Company maintains an insurance policy or policies providing liability insurance for directors, officers, employees, or agents or fiduciaries of the Company or of any other corporation, partnership, joint venture, trust, employee benefit plan or other enterprise that such person serves at the request of the Company, Indemnitee shall be covered by such policy or policies in accordance with its or their terms to the maximum extent of the coverage available for any director, officer, employee, agent or fiduciary under such policy or policies. If, at the time of the receipt of a notice of a claim pursuant to the terms hereof, the Company has director and officer liability insurance in effect, the Company shall give prompt notice of the commencement of such proceeding to the insurers in accordance with the procedures set forth in the respective policies. The Company shall thereafter take all necessary or desirable action to cause such insurers to pay, on behalf of the Indemnitee, all amounts payable as a result of such proceeding in accordance with the terms of such policies.

(c) The Company hereby acknowledges that Indemnitee has certain rights to indemnification, advancement of expenses and/or insurance provided by Abingworth LLP and certain of its affiliates (collectively, the "**Fund Indemnitors**"). The Company hereby agrees (i) that it is the indemnitor of first resort (i.e., its obligations to Indemnitee are primary and any obligation of the Fund Indemnitors to advance expenses or to provide indemnification for the same expenses or liabilities incurred by Indemnitee are secondary), (ii) that it shall be required to advance the full amount of expenses incurred by Indemnitee and shall be liable for the full amount of all Expenses, judgments, penalties, fines and amounts paid in settlement to the extent legally permitted and as required by the terms of this Agreement and the Certificate of Incorporation or Bylaws of the Company (or any other agreement between the Company and Indemnitee), without regard to any rights Indemnitee may have against the Fund Indemnitors, and (iii) that it irrevocably waives, relinquishes and releases the Fund Indemnitors from any and all claims against the Fund Indemnitors for contribution, subrogation or any other irrevocability of any kind in respect thereof. The Company further agrees that no advancement or payment by the Fund Indemnitors on behalf of Indemnitee with respect to any claim for which Indemnitee has sought indemnification from the

Company shall affect the foregoing and the Fund Indemnitors shall have a right of contribution and/or be subrogated to the extent of such advancement or payment to all of the rights of recovery of Indemnitee against the Company. The Company and Indemnitee agree that the Fund Indemnitors are express third party beneficiaries of the terms of this Section 8(c).

(d) Except as provided in paragraph (c) above, in the event of any payment under this Agreement, the Company shall be subrogated to the extent of such payment to all of the rights of recovery of Indemnitee, who shall execute all papers required and take all action necessary to secure such rights, including execution of such documents as are necessary to enable the Company to bring suit to enforce such rights.

(e) Except as provided in paragraph (c) above, the Company shall not be liable under this Agreement to make any payment of amounts otherwise indemnifiable hereunder if and to the extent that Indemnitee has otherwise actually received such payment under any insurance policy, contract, agreement or otherwise.

(f) Except as provided in paragraph (c) above, the Company's obligation to indemnify or advance Expenses hereunder to Indemnitee who is or was serving at the request of the Company as a director, officer, employee or agent of any other corporation, partnership, joint venture, trust, employee benefit plan or other enterprise shall be reduced by

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any amount Indemnitee has actually received as indemnification or advancement of expenses from such other corporation, partnership, joint venture, trust, employee benefit plan or other enterprise.

9. Exception to Right of Indemnification. Notwithstanding any provision in this Agreement, the Company shall not be obligated under this Agreement to make any indemnity in connection with any claim made against Indemnitee:

(a) for which payment has actually been made to or on behalf of Indemnitee under any insurance policy or other indemnity provision, except with respect to any excess beyond the amount paid under any insurance policy or other indemnity provision; or

(b) for an accounting of profits made from the purchase and sale (or sale and purchase) by Indemnitee of securities of the Company within the meaning of Section 16(b) of the Securities Exchange Act of 1934, as amended, or similar provisions of state statutory law or common law; or

(c) in connection with any Proceeding (or any part of any Proceeding) initiated by Indemnitee, including any Proceeding (or any part of any Proceeding) initiated by Indemnitee against the Company or its directors, officers, employees or other indemnitees, unless (i) the Board of Directors of the Company authorized the Proceeding (or any part of any Proceeding) prior to its initiation or (ii) the Company provides the indemnification, in its sole discretion, pursuant to the powers vested in the Company under applicable law.

10. Duration of Agreement. All agreements and obligations of the Company contained herein shall continue during the period Indemnitee is a director of the Company (or is or was serving at the request of the Company as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise) and for a period of five (5) years thereafter, and in addition shall continue thereafter so long as Indemnitee shall be subject to any Proceeding (or any proceeding commenced under Section 7 hereof) by reason of his Corporate Status, whether or not he is acting or serving in any such capacity at the time any liability or expense is incurred for which indemnification can be provided under this Agreement. This Agreement shall be binding upon and inure to the benefit of and be enforceable by the parties hereto and their respective successors (including any direct or indirect successor by purchase, merger, consolidation or otherwise to all or substantially all of the business or assets of the Company), assigns, spouses, heirs, executors and personal and legal representatives.

11. Security. To the extent requested by Indemnitee and approved by the Board of Directors of the Company, the Company may at any time and from time to time provide security to Indemnitee for the Company's obligations hereunder through an irrevocable bank line of credit, funded trust or other collateral. Any such security, once provided to Indemnitee, may not be revoked or released without the prior written consent of the Indemnitee.

12. Enforcement.

(a) The Company expressly confirms and agrees that it has entered into this Agreement and assumes the obligations imposed on it hereby in order to induce Indemnitee to serve as a director of the Company, and the Company acknowledges that Indemnitee is relying upon this Agreement in serving as a director of the Company.

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(b) This Agreement constitutes the entire agreement between the parties hereto with respect to the subject matter hereof and supersedes all prior agreements and understandings, oral, written and implied, between the parties hereto with respect to the subject matter hereof.

13. Definitions. For purposes of this Agreement:

(a) "**Corporate Status**" describes the status of a person who is or was a director, officer, employee, agent or fiduciary of the Company or of any other corporation, partnership, joint venture, trust, employee benefit plan or other enterprise that such person is or was serving at the express written request of the Company.

(b) "**Disinterested Director**" means a director of the Company who is not and was not a party to the Proceeding in respect of which indemnification is sought by Indemnitee.

(c) "**Enterprise**" shall mean the Company and any other corporation, partnership, joint venture, trust, employee benefit plan or other enterprise that Indemnitee is or was serving at the express written request of the Company as a director, officer, employee, agent or fiduciary.

(d) "**Expenses**" shall include all reasonable attorneys' fees, retainers, court costs, transcript costs, fees of experts, witness fees, travel expenses, duplicating costs, printing and binding costs, telephone charges, postage, delivery service fees and all other disbursements or expenses of the types customarily incurred in connection with prosecuting, defending, preparing to prosecute or defend, investigating, participating, or being or preparing to be a witness in a Proceeding. Expenses also shall include Expenses incurred in connection with any appeal resulting from any Proceeding, including without limitation the premium, security for, and other costs relating to any cost bond, supersedeas bond, or other appeal bond or its equivalent. Expenses, however, shall not include amounts paid in settlement by Indemnitee or the amount of judgments or fines against Indemnitee.

(e) **“Independent Counsel”** means a law firm, or a member of a law firm, that is experienced in matters of corporation law and neither presently is, nor in the past five years has been, retained to represent: (i) the Company or Indemnitee in any matter material to either such party (other than with respect to matters concerning Indemnitee under this Agreement, or of other indemnitees under similar indemnification agreements), or (ii) any other party to the Proceeding giving rise to a claim for indemnification hereunder. Notwithstanding the foregoing, the term “Independent Counsel” shall not include any person who, under the applicable standards of professional conduct then prevailing, would have a conflict of interest in representing either the Company or Indemnitee in an action to determine Indemnitee’s rights under this Agreement. The Company agrees to pay the reasonable fees of the Independent Counsel referred to above and to fully indemnify such counsel against any and all Expenses, claims, liabilities and damages arising out of or relating to this Agreement or its engagement pursuant hereto.

(f) **“Proceeding”** includes any threatened, pending or completed action, suit, arbitration, alternate dispute resolution mechanism, investigation, inquiry, administrative hearing or any other actual, threatened or completed proceeding, whether brought

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by or in the right of the Company or otherwise and whether civil, criminal, administrative or investigative, in which Indemnitee was, is or will be involved as a party or otherwise, by reason of the fact that Indemnitee is or was a director of the Company, by reason of any action taken by him or of any inaction on his part while acting as a director of the Company, or by reason of the fact that he is or was serving at the request of the Company as a director, officer, employee, agent or fiduciary of another corporation, partnership, joint venture, trust or other Enterprise; in each case whether or not he is acting or serving in any such capacity at the time any liability or expense is incurred for which indemnification can be provided under this Agreement; including one pending on or before the date of this Agreement, but excluding one initiated by an Indemnitee pursuant to Section 7 of this Agreement to enforce his rights under this Agreement.

14. **Severability.** The invalidity or unenforceability of any provision hereof shall in no way affect the validity or enforceability of any other provision. Without limiting the generality of the foregoing, this Agreement is intended to confer upon Indemnitee indemnification rights to the fullest extent permitted by applicable laws. In the event any provision hereof conflicts with any applicable law, such provision shall be deemed modified, consistent with the aforementioned intent, to the extent necessary to resolve such conflict.

15. **Modification and Waiver.** No supplement, modification, termination or amendment of this Agreement shall be binding unless executed in writing by both of the parties hereto. No waiver of any of the provisions of this Agreement shall be deemed or shall constitute a waiver of any other provisions hereof (whether or not similar) nor shall such waiver constitute a continuing waiver.

16. **Notice By Indemnitee.** Indemnitee agrees promptly to notify the Company in writing upon being served with or otherwise receiving any summons, citation, subpoena, complaint, indictment, information or other document relating to any Proceeding or matter which may be subject to indemnification covered hereunder. The failure to so notify the Company shall not relieve the Company of any obligation which it may have to Indemnitee under this Agreement or otherwise unless and only to the extent that such failure or delay materially prejudices the Company.

17. **Notices.** All notices and other communications given or made pursuant to this Agreement shall be in writing and shall be deemed effectively given: (a) upon personal delivery to the party to be notified, (b) when sent by confirmed electronic mail or facsimile if sent during normal business hours of the recipient, and if not so confirmed, then on the next business day, (c) five (5) days after having been sent by registered or certified mail, return receipt requested, postage prepaid, or (d) one (1) day after deposit with a nationally recognized overnight courier, specifying next day delivery, with written verification of receipt. All communications shall be sent:

(a) To Indemnitee at the address set forth below Indemnitee’s signature hereto.

(b) To the Company at:

200 West Street  
Waltham, MA 02451  
Attention: CEO

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or to such other address as may have been furnished to Indemnitee by the Company or to the Company by Indemnitee, as the case may be.

18. **Counterparts.** This Agreement may be executed in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same Agreement. This Agreement may also be executed and delivered by facsimile signature and in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument.

19. **Headings.** The headings of the paragraphs of this Agreement are inserted for convenience only and shall not be deemed to constitute part of this Agreement or to affect the construction thereof.

20. **Governing Law and Consent to Jurisdiction.** This Agreement and the legal relations among the parties shall be governed by, and construed and enforced in accordance with, the laws of the State of Delaware, without regard to its conflict of laws rules. The Company and Indemnitee hereby irrevocably and unconditionally (i) agree that any action or proceeding arising out of or in connection with this Agreement shall be brought only in the Chancery Court of the State of Delaware (the **“Delaware Court”**), and not in any other state or federal court in the United States of America or any court in any other country, (ii) consent to submit to the exclusive jurisdiction of the Delaware Court for purposes of any action or proceeding arising out of or in connection with this Agreement, (iii) waive any objection to the laying of venue of any such action or proceeding in the Delaware Court, and (iv) waive, and agree not to plead or to make, any claim that any such action or proceeding brought in the Delaware Court has been brought in an improper or inconvenient forum.

**SIGNATURE PAGE TO FOLLOW**

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**PROTEON THERAPEUTICS, INC.**

By: /s/ Timothy Noyes  
Name: Timothy Noyes  
Title: President and Chief Executive Officer

**INDEMNITEE**

/s/ Tim Haines  
Name: Tim Haines

Address:  
c/o Abingworth LLP  
38 Jermyn st.  
London, SW1Y 6DN  
United Kingdom

**SIGNATURE PAGE TO INDEMNIFICATION AGREEMENT - HAINES**

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**INDEMNIFICATION AGREEMENT**

**INDEMNIFICATION AGREEMENT**

THIS INDEMNIFICATION AGREEMENT (the “**Agreement**”) is made and entered into as of May 13, 2014 between **PROTEON THERAPEUTICS, INC.**, a Delaware corporation (the “**Company**”), and Dmitry Kobzyev (“**Indemnitee**”).

WITNESSETH THAT:

WHEREAS, highly competent persons have become more reluctant to serve corporations as directors or in other capacities unless they are provided with adequate protection through insurance or adequate indemnification against inordinate risks of claims and actions against them arising out of their service to and activities on behalf of the corporation;

WHEREAS, the Board of Directors of the Company (the “**Board**”) has determined that, in order to attract and retain qualified individuals, the Company will attempt to maintain on an ongoing basis, at its sole expense, liability insurance to protect persons serving the Company and its subsidiaries from certain liabilities. Although the furnishing of such insurance has been a customary and widespread practice among United States-based corporations and other business enterprises, the Company believes that, given current market conditions and trends, such insurance may be available to it in the future only at higher premiums and with more exclusions. At the same time, directors, officers, and other persons in service to corporations or business enterprises are being increasingly subjected to expensive and time-consuming litigation relating to, among other things, matters that traditionally would have been brought only against the Company or business enterprise itself. The Certificate of Incorporation of the Company permits, and the By-laws of the Company require, indemnification of directors of the Company. Indemnitee may also be entitled to indemnification pursuant to the General Corporation Law of the State of Delaware (“**DGCL**”). The By-laws and the DGCL expressly provide that the indemnification provisions set forth therein are not exclusive, and thereby contemplate that contracts may be entered into between the Company and members of the board of directors with respect to indemnification;

WHEREAS, the uncertainties relating to such insurance and to indemnification have increased the difficulty of attracting and retaining such persons;

WHEREAS, the Board has determined that the increased difficulty in attracting and retaining such persons is detrimental to the best interests of the Company’s stockholders and that the Company should act to assure such persons that there will be increased certainty of such protection in the future;

WHEREAS, it is reasonable, prudent and necessary for the Company contractually to obligate itself to indemnify, and to advance expenses on behalf of, such persons to the fullest extent permitted by applicable law so that they will serve or continue to serve the Company free from undue concern that they will not be so indemnified;

WHEREAS, this Agreement is a supplement to and in furtherance of the By-laws of the Company and any resolutions adopted pursuant thereto, and shall not be deemed a substitute therefor, nor to diminish or abrogate any rights of Indemnitee thereunder;

WHEREAS, Indemnitee does not regard the protection available under the Company’s By-laws and insurance as adequate in the present circumstances, and may not be willing to serve as a director without adequate protection, and the Company desires Indemnitee to serve in such capacity. Indemnitee is willing to serve, continue to serve and to take on additional service for or on behalf of the Company on the condition that he be so indemnified; and

NOW, THEREFORE, in consideration of Indemnitee’s agreement to serve as a director after the date hereof, the parties hereto agree as follows:

1. Indemnity of Indemnitee. The Company hereby agrees to hold harmless and indemnify Indemnitee to the fullest extent permitted by law, as such may be amended from time to time. In furtherance of the foregoing indemnification, and without limiting the generality thereof:

(a) Proceedings Other Than Proceedings by or in the Right of the Company. Indemnitee shall be entitled to the rights of indemnification provided in this Section 1(a) if, by reason of his Corporate Status (as hereinafter defined), the Indemnitee is, or is threatened to be made, a party to or participant in any Proceeding (as hereinafter defined) other than a Proceeding by or in the right of the Company. Pursuant to this Section 1(a), Indemnitee shall be indemnified against all Expenses (as hereinafter defined), judgments, penalties, fines and amounts paid in settlement actually and reasonably incurred by him, or on his behalf, in connection with such Proceeding or any claim, issue or matter therein, if the Indemnitee acted in good faith and in a manner the Indemnitee reasonably believed to be in or not opposed to the best interests of the Company, and with respect to any criminal Proceeding, had no reasonable cause to believe the Indemnitee’s conduct was unlawful.

(b) Proceedings by or in the Right of the Company. Indemnitee shall be entitled to the rights of indemnification provided in this Section 1(b) if, by reason of his Corporate Status, the Indemnitee is, or is threatened to be made, a party to or participant in any Proceeding brought by or in the right of the Company. Pursuant to this Section 1(b), Indemnitee shall be indemnified against all Expenses actually and reasonably incurred by the Indemnitee, or on the Indemnitee’s behalf, in connection with such Proceeding if the Indemnitee acted in good faith and in a manner the Indemnitee reasonably believed to be in or not opposed to the best interests of the Company; provided, however, if applicable law so provides, no indemnification against such Expenses shall be made in respect of any claim, issue or matter in such Proceeding as to which Indemnitee shall have been adjudged to be liable to the Company unless and to the extent that the Court of Chancery of the State of Delaware shall determine that such indemnification may be made.

(c) Indemnification for Expenses of a Party Who is Wholly or Partly Successful. Notwithstanding any other provision of this Agreement, to the extent that Indemnitee is, by reason of his Corporate Status, a party to and is successful, on the merits or otherwise, in any Proceeding, he shall be indemnified to the maximum extent permitted by law, as such may be amended from time to time, against all Expenses actually and reasonably incurred by him or on his behalf in connection therewith. If Indemnitee is not wholly successful in such Proceeding but is successful, on the merits or otherwise, as to one or more but less than all claims, issues or matters in such Proceeding, the Company shall indemnify Indemnitee against all Expenses actually and reasonably incurred by him or on his behalf in connection with each successfully resolved claim, issue or matter. For purposes of this Section and without

limitation, the termination of any claim, issue or matter in such a Proceeding by dismissal, with or without prejudice, shall be deemed to be a successful result as to such claim, issue or matter.

2. Additional Indemnity. In addition to, and without regard to any limitations on, the indemnification provided for in Section 1 of this Agreement, the Company shall and hereby does indemnify and hold harmless Indemnitee against all Expenses, judgments, penalties, fines and amounts paid in settlement actually and reasonably incurred by him or on his behalf if, by reason of his Corporate Status, he is, or is threatened to be made, a party to or participant in any Proceeding (including a Proceeding by or in the right of the Company), including, without limitation, all liability arising out of the negligence or active or passive wrongdoing of Indemnitee. The only limitation that shall exist upon the Company's obligations pursuant to this Agreement shall be that the Company shall not be obligated to make any payment to Indemnitee that is finally determined (under the procedures, and subject to the presumptions, set forth in Sections 6 and 7 hereof) to be unlawful.

3. Contribution.

(a) Whether or not the indemnification provided in Sections 1 and 2 hereof is available, in respect of any threatened, pending or completed action, suit or proceeding in which the Company is jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding), the Company shall pay, in the first instance, the entire amount of any judgment or settlement of such action, suit or proceeding without requiring Indemnitee to contribute to such payment and the Company hereby waives and relinquishes any right of contribution it may have against Indemnitee. The Company shall not enter into any settlement of any action, suit or proceeding in which the Company is jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding) unless such settlement provides for a full and final release of all claims asserted against Indemnitee.

(b) Without diminishing or impairing the obligations of the Company set forth in the preceding subparagraph, if, for any reason, Indemnitee shall elect or be required to pay all or any portion of any judgment or settlement in any threatened, pending or completed action, suit or proceeding in which the Company is jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding), the Company shall contribute to the amount of expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred and paid or payable by Indemnitee in proportion to the relative benefits received by the Company and all officers, directors or employees of the Company, other than Indemnitee, who are jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding), on the one hand, and Indemnitee, on the other hand, from the transaction from which such action, suit or proceeding arose; provided, however, that the proportion determined on the basis of relative benefit may, to the extent necessary to conform to law, be further adjusted by reference to the relative fault of the Company and all officers, directors or employees of the Company other than Indemnitee who are jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding), on the one hand, and Indemnitee, on the other hand, in connection with the events that resulted in such expenses, judgments, fines or settlement amounts, as well as any other equitable considerations which the Law may require to be considered. The relative fault of the Company and all officers, directors or employees of the Company, other than Indemnitee, who are jointly liable with Indemnitee (or would be if joined in such action, suit or proceeding), on the one hand, and Indemnitee, on the other hand, shall be determined by reference to, among other things, the degree to which their actions were motivated

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by intent to gain personal profit or advantage, the degree to which their liability is primary or secondary and the degree to which their conduct is active or passive.

(c) The Company hereby agrees to fully indemnify and hold Indemnitee harmless from any claims of contribution which may be brought by officers, directors or employees of the Company, other than Indemnitee, who may be jointly liable with Indemnitee.

(d) To the fullest extent permissible under applicable law, if the indemnification provided for in this Agreement is unavailable to Indemnitee for any reason whatsoever, the Company, in lieu of indemnifying Indemnitee, shall contribute to the amount incurred by Indemnitee, whether for judgments, fines, penalties, excise taxes, amounts paid or to be paid in settlement and/or for Expenses, in connection with any claim relating to an indemnifiable event under this Agreement, in such proportion as is deemed fair and reasonable in light of all of the circumstances of such Proceeding in order to reflect (i) the relative benefits received by the Company and Indemnitee as a result of the event(s) and/or transaction(s) giving cause to such Proceeding; and/or (ii) the relative fault of the Company (and its directors, officers, employees and agents) and Indemnitee in connection with such event(s) and/or transaction(s).

4. Indemnification for Expenses of a Witness. Notwithstanding any other provision of this Agreement, to the extent that Indemnitee is, by reason of his Corporate Status, a witness in any Proceeding to which Indemnitee is not a party, he shall be indemnified against all Expenses actually and reasonably incurred by him or on his behalf in connection therewith.

5. Advancement of Expenses. Notwithstanding any other provision of this Agreement, the Company shall advance all Expenses incurred by or on behalf of Indemnitee in connection with any Proceeding by reason of Indemnitee's Corporate Status within thirty (30) days after the receipt by the Company of a statement or statements from Indemnitee requesting such advance or advances from time to time, whether prior to or after final disposition of such Proceeding. Such statement or statements shall reasonably evidence the Expenses incurred by Indemnitee and shall include or be preceded or accompanied by an undertaking by or on behalf of Indemnitee to repay any Expenses advanced if it shall ultimately be determined that Indemnitee is not entitled to be indemnified against such Expenses. Any advances and undertakings to repay pursuant to this Section 5 shall be unsecured and interest free.

6. Procedures and Presumptions for Determination of Entitlement to Indemnification. It is the intent of this Agreement to secure for Indemnitee rights of indemnity that are as favorable as may be permitted under the Delaware General Corporation Law and public policy of the State of Delaware. Accordingly, the parties agree that the following procedures and presumptions shall apply in the event of any question as to whether Indemnitee is entitled to indemnification under this Agreement:

(a) To obtain indemnification under this Agreement, Indemnitee shall submit to the Company a written request, including therein or therewith such documentation and information as is reasonably available to Indemnitee and is reasonably necessary to determine whether and to what extent Indemnitee is entitled to indemnification. The Secretary of the Company shall, promptly upon receipt of such a request for indemnification, advise the Board of Directors in writing that Indemnitee has requested indemnification.

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(b) Upon written request by Indemnitee for indemnification pursuant to the first sentence of Section 6(a) hereof, a determination, if required by applicable law, with respect to Indemnitee's entitlement thereto shall be made in the specific case by one of the following three methods, which shall be

at the election of the board: (1) by a majority vote of the disinterested directors, even though less than a quorum, by a committee of disinterested directors designated by a majority vote of the disinterested directors, even though less than a quorum, (2) if there are no disinterested directors or if the disinterested directors so direct, by independent legal counsel in a written opinion to the Board of Directors, a copy of which shall be delivered to the Indemnitee, or (3) if so directed by the Board of Directors, by the stockholders of the Company. For purposes hereof, disinterested directors are those members of the board of directors of the Company who are not parties to the action, suit or proceeding in respect of which indemnification is sought by Indemnitee.

(c) If the determination of entitlement to indemnification is to be made by Independent Counsel pursuant to Section 6(b) hereof, the Independent Counsel shall be selected as provided in this Section 6(c). The determination of whether Independent Counsel shall be engaged and the selection of such Independent Counsel shall be made by the Board of Directors. Indemnitee may, within 10 days after such written notice of selection shall have been given, deliver to the Company, as the case may be, a written objection to such selection; provided, however, that such objection may be asserted only on the ground that the Independent Counsel so selected does not meet the requirements of “**Independent Counsel**” as defined in Section 13 of this Agreement, and the objection shall set forth with particularity the factual basis of such assertion. Absent a proper and timely objection, the person so selected shall act as Independent Counsel. If a written objection is made and substantiated, the Independent Counsel selected may not serve as Independent Counsel unless and until such objection is withdrawn or a court has determined that such objection is without merit. If, within 20 days after submission by Indemnitee of a written request for indemnification pursuant to Section 6(a) hereof, no Independent Counsel shall have been selected and not objected to, either the Company or Indemnitee may petition the Court of Chancery of the State of Delaware or other court of competent jurisdiction for resolution of any objection which shall have been made by the Indemnitee to the Company’s selection of Independent Counsel and/or for the appointment as Independent Counsel of a person selected by the court or by such other person as the court shall designate, and the person with respect to whom all objections are so resolved or the person so appointed shall act as Independent Counsel under Section 6(b) hereof. The Company shall pay any and all reasonable fees and expenses of Independent Counsel incurred by such Independent Counsel in connection with acting pursuant to Section 6(b) hereof, and the Company shall pay all reasonable fees and expenses incident to the procedures of this Section 6(c), regardless of the manner in which such Independent Counsel was selected or appointed.

(d) In making a determination with respect to entitlement to indemnification hereunder, the person or persons or entity making such determination shall presume that Indemnitee is entitled to indemnification under this Agreement. Anyone seeking to overcome this presumption shall have the burden of proof and the burden of persuasion by clear and convincing evidence. Neither the failure of the Company (including by its directors or independent legal counsel) to have made a determination prior to the commencement of any action pursuant to this Agreement that indemnification is proper in the circumstances because Indemnitee has met the applicable standard of conduct, nor an actual determination by the Company (including by its directors or independent legal counsel) that Indemnitee has not met

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such applicable standard of conduct, shall be a defense to the action or create a presumption that Indemnitee has not met the applicable standard of conduct.

(e) Indemnitee shall be deemed to have acted in good faith if Indemnitee’s action is based on the records or books of account of the Enterprise (as hereinafter defined), including financial statements, or on information supplied to Indemnitee by the officers of the Enterprise in the course of their duties, or on the advice of legal counsel for the Enterprise or on information or records given or reports made to the Enterprise by an independent certified public accountant or by an appraiser or other expert selected with reasonable care by the Enterprise. In addition, the knowledge and/or actions, or failure to act, of any director, officer, agent or employee of the Enterprise shall not be imputed to Indemnitee for purposes of determining the right to indemnification under this Agreement. Whether or not the foregoing provisions of this Section 6(e) are satisfied, it shall in any event be presumed that Indemnitee has at all times acted in good faith and in a manner he reasonably believed to be in or not opposed to the best interests of the Company. Anyone seeking to overcome this presumption shall have the burden of proof and the burden of persuasion by clear and convincing evidence.

(f) If the person, persons or entity empowered or selected under Section 6 to determine whether Indemnitee is entitled to indemnification shall not have made a determination within sixty (60) days after receipt by the Company of the request therefor, the requisite determination of entitlement to indemnification shall be deemed to have been made and Indemnitee shall be entitled to such indemnification absent (i) a misstatement by Indemnitee of a material fact, or an omission of a material fact necessary to make Indemnitee’s statement not materially misleading, in connection with the request for indemnification, or (ii) a prohibition of such indemnification under applicable law; provided, however, that such 60-day period may be extended for a reasonable time, not to exceed an additional thirty (30) days, if the person, persons or entity making such determination with respect to entitlement to indemnification in good faith requires such additional time to obtain or evaluate documentation and/or information relating thereto; and provided, further, that the foregoing provisions of this Section 6(f) shall not apply if the determination of entitlement to indemnification is to be made by the stockholders pursuant to Section 6(b) of this Agreement and if (A) within fifteen (15) days after receipt by the Company of the request for such determination, the Board of Directors or the Disinterested Directors, if appropriate, resolve to submit such determination to the stockholders for their consideration at an annual meeting thereof to be held within seventy-five (75) days after such receipt and such determination is made thereat, or (B) a special meeting of stockholders is called within fifteen (15) days after such receipt for the purpose of making such determination, such meeting is held for such purpose within sixty (60) days after having been so called and such determination is made thereat.

(g) Indemnitee shall cooperate with the person, persons or entity making such determination with respect to Indemnitee’s entitlement to indemnification, including providing to such person, persons or entity upon reasonable advance request any documentation or information which is not privileged or otherwise protected from disclosure and which is reasonably available to Indemnitee and reasonably necessary to such determination. Any Independent Counsel, member of the Board of Directors or stockholder of the Company shall act reasonably and in good faith in making a determination regarding the Indemnitee’s entitlement to indemnification under this Agreement. Any costs or expenses (including attorneys’ fees and disbursements) incurred by Indemnitee in so cooperating with the person,

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persons or entity making such determination shall be borne by the Company (irrespective of the determination as to Indemnitee’s entitlement to indemnification) and the Company hereby indemnifies and agrees to hold Indemnitee harmless therefrom.

(h) The Company acknowledges that a settlement or other disposition short of final judgment may be successful if it permits a party to avoid expense, delay, distraction, disruption and uncertainty. In the event that any action, claim or proceeding to which Indemnitee is a party is resolved in any manner other than by adverse judgment against Indemnitee (including, without limitation, settlement of such action, claim or proceeding with or without payment of money or other consideration) it shall be presumed that Indemnitee has been successful on the merits or otherwise in such action, suit or proceeding. Anyone seeking to overcome this presumption shall have the burden of proof and the burden of persuasion by clear and convincing evidence.

(i) The termination of any Proceeding or of any claim, issue or matter therein, by judgment, order, settlement or conviction, or upon a plea of nolo contendere or its equivalent, shall not (except as otherwise expressly provided in this Agreement) of itself adversely affect the right of Indemnitee to

indemnification or create a presumption that Indemnitee did not act in good faith and in a manner which he reasonably believed to be in or not opposed to the best interests of the Company or, with respect to any criminal Proceeding, that Indemnitee had reasonable cause to believe that his conduct was unlawful.

7. Remedies of Indemnitee.

(a) In the event that (i) a determination is made pursuant to Section 6 of this Agreement that Indemnitee is not entitled to indemnification under this Agreement, (ii) advancement of Expenses is not timely made pursuant to Section 5 of this Agreement, (iii) no determination of entitlement to indemnification is made pursuant to Section 6(b) of this Agreement within 90 days after receipt by the Company of the request for indemnification, (iv) payment of indemnification is not made pursuant to this Agreement within ten (10) days after receipt by the Company of a written request therefor or (v) payment of indemnification is not made within ten (10) days after a determination has been made that Indemnitee is entitled to indemnification or such determination is deemed to have been made pursuant to Section 6 of this Agreement, Indemnitee shall be entitled to an adjudication in an appropriate court of the State of Delaware, or in any other court of competent jurisdiction, of Indemnitee's entitlement to such indemnification. Indemnitee shall commence such proceeding seeking an adjudication within 180 days following the date on which Indemnitee first has the right to commence such proceeding pursuant to this Section 7(a). The Company shall not oppose Indemnitee's right to seek any such adjudication.

(b) In the event that a determination shall have been made pursuant to Section 6(b) of this Agreement that Indemnitee is not entitled to indemnification, any judicial proceeding commenced pursuant to this Section 7 shall be conducted in all respects as a de novo trial on the merits, and Indemnitee shall not be prejudiced by reason of the adverse determination under Section 6(b).

(c) If a determination shall have been made pursuant to Section 6(b) of this Agreement that Indemnitee is entitled to indemnification, the Company shall be bound by such determination in any judicial proceeding commenced pursuant to this Section 7, absent (i) a

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misstatement by Indemnitee of a material fact, or an omission of a material fact necessary to make Indemnitee's statement not materially misleading in connection with the application for indemnification, or (ii) a prohibition of such indemnification under applicable law.

(d) In the event that Indemnitee, pursuant to this Section 7, seeks a judicial adjudication of his rights under, or to recover damages for breach of, this Agreement, or to recover under any directors' and officers' liability insurance policies maintained by the Company, the Company shall pay on his behalf, in advance, any and all expenses (of the types described in the definition of Expenses in Section 13 of this Agreement) actually and reasonably incurred by him in such judicial adjudication, regardless of whether Indemnitee ultimately is determined to be entitled to such indemnification, advancement of expenses or insurance recovery.

(e) The Company shall be precluded from asserting in any judicial proceeding commenced pursuant to this Section 7 that the procedures and presumptions of this Agreement are not valid, binding and enforceable and shall stipulate in any such court that the Company is bound by all the provisions of this Agreement. The Company shall indemnify Indemnitee against any and all Expenses and, if requested by Indemnitee, shall (within ten (10) days after receipt by the Company of a written request therefore) advance, to the extent not prohibited by law, such expenses to Indemnitee, which are incurred by Indemnitee in connection with any action brought by Indemnitee for indemnification or advance of Expenses from the Company under this Agreement or under any directors' and officers' liability insurance policies maintained by the Company, regardless of whether Indemnitee ultimately is determined to be entitled to such indemnification, advancement of Expenses or insurance recovery, as the case may be.

(f) Notwithstanding anything in this Agreement to the contrary, no determination as to entitlement to indemnification under this Agreement shall be required to be made prior to the final disposition of the Proceeding.

8. Non-Exclusivity; Survival of Rights; Insurance; Primacy of Indemnification; Subrogation.

(a) The rights of indemnification as provided by this Agreement shall not be deemed exclusive of any other rights to which Indemnitee may at any time be entitled under applicable law, the certificate of incorporation of the Company, the Bylaws, any agreement, a vote of stockholders, a resolution of directors or otherwise. No amendment, alteration or repeal of this Agreement or of any provision hereof shall limit or restrict any right of Indemnitee under this Agreement in respect of any action taken or omitted by such Indemnitee in his Corporate Status prior to such amendment, alteration or repeal. To the extent that a change in the Delaware General Corporation Law, whether by statute or judicial decision, permits greater indemnification than would be afforded currently under the Bylaws and this Agreement, it is the intent of the parties hereto that Indemnitee shall enjoy by this Agreement the greater benefits so afforded by such change. No right or remedy herein conferred is intended to be exclusive of any other right or remedy, and every other right and remedy shall be cumulative and in addition to every other right and remedy given hereunder or now or hereafter existing at law or in equity or otherwise. The assertion or employment of any right or remedy hereunder, or otherwise, shall not prevent the concurrent assertion or employment of any other right or remedy.

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(b) To the extent that the Company maintains an insurance policy or policies providing liability insurance for directors, officers, employees, or agents or fiduciaries of the Company or of any other corporation, partnership, joint venture, trust, employee benefit plan or other enterprise that such person serves at the request of the Company, Indemnitee shall be covered by such policy or policies in accordance with its or their terms to the maximum extent of the coverage available for any director, officer, employee, agent or fiduciary under such policy or policies. If, at the time of the receipt of a notice of a claim pursuant to the terms hereof, the Company has director and officer liability insurance in effect, the Company shall give prompt notice of the commencement of such proceeding to the insurers in accordance with the procedures set forth in the respective policies. The Company shall thereafter take all necessary or desirable action to cause such insurers to pay, on behalf of the Indemnitee, all amounts payable as a result of such proceeding in accordance with the terms of such policies.

(c) The Company hereby acknowledges that Indemnitee has certain rights to indemnification, advancement of expenses and/or insurance provided by Pharmstandard Internation S.A., with registered address 65, Boulevard Grande-Duchesse Charlotte L - 1331 Luxembourg, and certain of its affiliates (collectively, the "**Fund Indemnitors**"). The Company hereby agrees (i) that it is the indemnitor of first resort (i.e., its obligations to Indemnitee are primary and any obligation of the Fund Indemnitors to advance expenses or to provide indemnification for the same expenses or liabilities incurred by Indemnitee are secondary), (ii) that it shall be required to advance the full amount of expenses incurred by Indemnitee and shall be liable for the full amount of all Expenses, judgments, penalties, fines and amounts paid in settlement to the extent legally permitted and as required by the terms of this Agreement and the Certificate of Incorporation or Bylaws of the Company (or any other agreement between the Company and Indemnitee), without regard to any rights Indemnitee may have against the Fund Indemnitors, and (iii) that it irrevocably waives, relinquishes and releases the Fund Indemnitors from any and all claims against the Fund Indemnitors for contribution, subrogation or any other recovery of any kind in respect thereof. The Company further agrees that no advancement or payment by the Fund Indemnitors

on behalf of Indemnitee with respect to any claim for which Indemnitee has sought indemnification from the Company shall affect the foregoing and the Fund Indemnitors shall have a right of contribution and/or be subrogated to the extent of such advancement or payment to all of the rights of recovery of Indemnitee against the Company. The Company and Indemnitee agree that the Fund Indemnitors are express third party beneficiaries of the terms of this Section 8(c).

(d) Except as provided in paragraph (c) above, in the event of any payment under this Agreement, the Company shall be subrogated to the extent of such payment to all of the rights of recovery of Indemnitee, who shall execute all papers required and take all action necessary to secure such rights, including execution of such documents as are necessary to enable the Company to bring suit to enforce such rights.

(e) Except as provided in paragraph (c) above, the Company shall not be liable under this Agreement to make any payment of amounts otherwise indemnifiable hereunder if and to the extent that Indemnitee has otherwise actually received such payment under any insurance policy, contract, agreement or otherwise.

(f) Except as provided in paragraph (c) above, the Company's obligation to indemnify or advance Expenses hereunder to Indemnitee who is or was serving at the request of the Company as a director, officer, employee or agent of any other corporation,

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partnership, joint venture, trust, employee benefit plan or other enterprise shall be reduced by any amount Indemnitee has actually received as indemnification or advancement of expenses from such other corporation, partnership, joint venture, trust, employee benefit plan or other enterprise.

9. Exception to Right of Indemnification. Notwithstanding any provision in this Agreement, the Company shall not be obligated under this Agreement to make any indemnity in connection with any claim made against Indemnitee:

(a) for which payment has actually been made to or on behalf of Indemnitee under any insurance policy or other indemnity provision, except with respect to any excess beyond the amount paid under any insurance policy or other indemnity provision; or

(b) for an accounting of profits made from the purchase and sale (or sale and purchase) by Indemnitee of securities of the Company within the meaning of Section 16(b) of the Securities Exchange Act of 1934, as amended, or similar provisions of state statutory law or common law; or

(c) in connection with any Proceeding (or any part of any Proceeding) initiated by Indemnitee, including any Proceeding (or any part of any Proceeding) initiated by Indemnitee against the Company or its directors, officers, employees or other indemnitees, unless (i) the Board of Directors of the Company authorized the Proceeding (or any part of any Proceeding) prior to its initiation or (ii) the Company provides the indemnification, in its sole discretion, pursuant to the powers vested in the Company under applicable law.

10. Duration of Agreement. All agreements and obligations of the Company contained herein shall continue during the period Indemnitee is a director of the Company (or is or was serving at the request of the Company as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise) and for a period of five (5) years thereafter, and in addition shall continue thereafter so long as Indemnitee shall be subject to any Proceeding (or any proceeding commenced under Section 7 hereof) by reason of his Corporate Status, whether or not he is acting or serving in any such capacity at the time any liability or expense is incurred for which indemnification can be provided under this Agreement. This Agreement shall be binding upon and inure to the benefit of and be enforceable by the parties hereto and their respective successors (including any direct or indirect successor by purchase, merger, consolidation or otherwise to all or substantially all of the business or assets of the Company), assigns, spouses, heirs, executors and personal and legal representatives.

11. Security. To the extent requested by Indemnitee and approved by the Board of Directors of the Company, the Company may at any time and from time to time provide security to Indemnitee for the Company's obligations hereunder through an irrevocable bank line of credit, funded trust or other collateral. Any such security, once provided to Indemnitee, may not be revoked or released without the prior written consent of the Indemnitee.

12. Enforcement.

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(a) The Company expressly confirms and agrees that it has entered into this Agreement and assumes the obligations imposed on it hereby in order to induce Indemnitee to serve as a director of the Company, and the Company acknowledges that Indemnitee is relying upon this Agreement in serving as a director of the Company.

(b) This Agreement constitutes the entire agreement between the parties hereto with respect to the subject matter hereof and supersedes all prior agreements and understandings, oral, written and implied, between the parties hereto with respect to the subject matter hereof.

13. Definitions. For purposes of this Agreement:

(a) "**Corporate Status**" describes the status of a person who is or was a director, officer, employee, agent or fiduciary of the Company or of any other corporation, partnership, joint venture, trust, employee benefit plan or other enterprise that such person is or was serving at the express written request of the Company.

(b) "**Disinterested Director**" means a director of the Company who is not and was not a party to the Proceeding in respect of which indemnification is sought by Indemnitee.

(c) "**Enterprise**" shall mean the Company and any other corporation, partnership, joint venture, trust, employee benefit plan or other enterprise that Indemnitee is or was serving at the express written request of the Company as a director, officer, employee, agent or fiduciary.

(d) "**Expenses**" shall include all reasonable attorneys' fees, retainers, court costs, transcript costs, fees of experts, witness fees, travel expenses, duplicating costs, printing and binding costs, telephone charges, postage, delivery service fees and all other disbursements or expenses of the types customarily incurred in connection with prosecuting, defending, preparing to prosecute or defend, investigating, participating, or being or preparing to be a witness in a Proceeding. Expenses also shall include Expenses incurred in connection with any appeal resulting from any Proceeding, including without limitation the premium, security for, and other costs relating to any cost bond, supersedeas bond, or other appeal bond or its equivalent. Expenses, however, shall not include amounts paid in settlement by Indemnitee or the amount of judgments or fines against Indemnitee.

(e) **“Independent Counsel”** means a law firm, or a member of a law firm, that is experienced in matters of corporation law and neither presently is, nor in the past five years has been, retained to represent: (i) the Company or Indemnitee in any matter material to either such party (other than with respect to matters concerning Indemnitee under this Agreement, or of other indemnitees under similar indemnification agreements), or (ii) any other party to the Proceeding giving rise to a claim for indemnification hereunder. Notwithstanding the foregoing, the term “Independent Counsel” shall not include any person who, under the applicable standards of professional conduct then prevailing, would have a conflict of interest in representing either the Company or Indemnitee in an action to determine Indemnitee’s rights under this Agreement. The Company agrees to pay the reasonable fees of the Independent Counsel referred to above and to fully indemnify such counsel against any and all Expenses,

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claims, liabilities and damages arising out of or relating to this Agreement or its engagement pursuant hereto.

(f) **“Proceeding”** includes any threatened, pending or completed action, suit, arbitration, alternate dispute resolution mechanism, investigation, inquiry, administrative hearing or any other actual, threatened or completed proceeding, whether brought by or in the right of the Company or otherwise and whether civil, criminal, administrative or investigative, in which Indemnitee was, is or will be involved as a party or otherwise, by reason of the fact that Indemnitee is or was a director of the Company, by reason of any action taken by him or of any inaction on his part while acting as a director of the Company, or by reason of the fact that he is or was serving at the request of the Company as a director, officer, employee, agent or fiduciary of another corporation, partnership, joint venture, trust or other Enterprise; in each case whether or not he is acting or serving in any such capacity at the time any liability or expense is incurred for which indemnification can be provided under this Agreement; including one pending on or before the date of this Agreement, but excluding one initiated by an Indemnitee pursuant to Section 7 of this Agreement to enforce his rights under this Agreement.

14. **Severability.** The invalidity or unenforceability of any provision hereof shall in no way affect the validity or enforceability of any other provision. Without limiting the generality of the foregoing, this Agreement is intended to confer upon Indemnitee indemnification rights to the fullest extent permitted by applicable laws. In the event any provision hereof conflicts with any applicable law, such provision shall be deemed modified, consistent with the aforementioned intent, to the extent necessary to resolve such conflict.

15. **Modification and Waiver.** No supplement, modification, termination or amendment of this Agreement shall be binding unless executed in writing by both of the parties hereto. No waiver of any of the provisions of this Agreement shall be deemed or shall constitute a waiver of any other provisions hereof (whether or not similar) nor shall such waiver constitute a continuing waiver.

16. **Notice By Indemnitee.** Indemnitee agrees promptly to notify the Company in writing upon being served with or otherwise receiving any summons, citation, subpoena, complaint, indictment, information or other document relating to any Proceeding or matter which may be subject to indemnification covered hereunder. The failure to so notify the Company shall not relieve the Company of any obligation which it may have to Indemnitee under this Agreement or otherwise unless and only to the extent that such failure or delay materially prejudices the Company.

17. **Notices.** All notices and other communications given or made pursuant to this Agreement shall be in writing and shall be deemed effectively given: (a) upon personal delivery to the party to be notified, (b) when sent by confirmed electronic mail or facsimile if sent during normal business hours of the recipient, and if not so confirmed, then on the next business day, (c) five (5) days after having been sent by registered or certified mail, return receipt requested, postage prepaid, or (d) one (1) day after deposit with a nationally recognized overnight courier, specifying next day delivery, with written verification of receipt. All communications shall be sent:

(a) To Indemnitee at the address set forth below Indemnitee’s signature hereto.

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(b) To the Company at:

200 West Street  
Waltham, MA 02451  
Attention: CEO

or to such other address as may have been furnished to Indemnitee by the Company or to the Company by Indemnitee, as the case may be.

18. **Counterparts.** This Agreement may be executed in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same Agreement. This Agreement may also be executed and delivered by facsimile signature and in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument.

19. **Headings.** The headings of the paragraphs of this Agreement are inserted for convenience only and shall not be deemed to constitute part of this Agreement or to affect the construction thereof.

20. **Governing Law and Consent to Jurisdiction.** This Agreement and the legal relations among the parties shall be governed by, and construed and enforced in accordance with, the laws of the State of Delaware, without regard to its conflict of laws rules. The Company and Indemnitee hereby irrevocably and unconditionally (i) agree that any action or proceeding arising out of or in connection with this Agreement shall be brought only in the Chancery Court of the State of Delaware (the **“Delaware Court”**), and not in any other state or federal court in the United States of America or any court in any other country, (ii) consent to submit to the exclusive jurisdiction of the Delaware Court for purposes of any action or proceeding arising out of or in connection with this Agreement, (iii) waive any objection to the laying of venue of any such action or proceeding in the Delaware Court, and (iv) waive, and agree not to plead or to make, any claim that any such action or proceeding brought in the Delaware Court has been brought in an improper or inconvenient forum.

**SIGNATURE PAGE TO FOLLOW**

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IN WITNESS WHEREOF, the parties hereto have executed this Indemnification Agreement on and as of the day and year first above written.

**PROTEON THERAPEUTICS, INC.**

By: /s/ Timothy Noyes

Name: Timothy Noyes

Title: President and Chief Executive Officer

**INDEMNITEE**

/s/ Dmitry Kobzyev

Name: Dmitry Kobzyev

Address:

115172, Moscow Russia

Krasncholmskaya nub 13 Bld 1, 2

**SIGNATURE PAGE TO INDEMNIFICATION AGREEMENT - KOBYZEV**

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Subsidiaries of Proteon Therapeutics, Inc.

Name of Subsidiary	Jurisdiction	Ownership Percentage
Proteon Therapeutics, Ltd.	UK	100%