

UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
WASHINGTON, DC 20549

AMENDMENT NO. 1  
TO  
FORM S-3  
REGISTRATION STATEMENT  
UNDER  
*THE SECURITIES ACT OF 1933*

**PROTEON THERAPEUTICS, INC.**  
(Exact name of registrant as specified in its charter)

**Delaware**  
(State or other jurisdiction of  
incorporation or organization)

**20-4580525**  
(IRS Employer  
Identification Number)

**200 West Street**  
**Waltham, Massachusetts 02451**  
**(781) 890-0102**  
(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

**Timothy P. Noyes**  
**Chief Executive Officer, President and Director**  
**Proteon Therapeutics, Inc.**  
**200 West Street**  
**Waltham, Massachusetts 02451**  
**(781) 890-0102**  
(Name, address, including zip code, and telephone number, including area code, of agent for service)

*Copy to:*  
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Approximate date of commencement of proposed sale to the public:  
**From time to time after the effective date of this Registration Statement.**

If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box.

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 of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, 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, please 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, please 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 registration statement pursuant to General Instruction I.D. or a post-effective amendment thereto that shall become effective upon filing with the Commission pursuant to Rule 462(e) under the Securities Act, check the following box.

If this Form is a post-effective amendment to a registration statement filed pursuant to General Instruction I.D. filed to register additional securities or additional classes of securities pursuant to Rule 413(b) under the Securities Act, check the following box.

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 Securities Exchange Act of 1934.

Large accelerated filer	<input type="checkbox"/>	Accelerated filer	<input checked="" type="checkbox"/>
Non-accelerated filer	<input type="checkbox"/> (Do not check if a smaller reporting company)	Smaller reporting company	<input type="checkbox"/>
		Emerging growth company	<input checked="" type="checkbox"/>

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of Securities Act.

**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 this Registration Statement shall become effective on such date as the Securities and Exchange Commission, acting pursuant to such Section 8(a), may determine.**

**The information contained in this prospectus is not complete and may be changed. The selling stockholders named in this prospectus may not sell these securities until the Registration Statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and is not a solicitation of offers to buy these securities in any jurisdiction where such offer or sale is not permitted.**

**Subject to Completion, dated August 14, 2017**

**Prospectus**



**22,112,775 Shares of Common Stock**

This prospectus relates to the possible resale, from time to time, by the selling stockholders identified in this prospectus of up to 22,112,775 shares of our common stock, par value \$0.001 per share, issuable upon conversion of our Series A Convertible Preferred Stock (subject to adjustment as set forth in the Certificate of Designation of Preferences, Rights and Limitations of Series A Convertible Preferred Stock), initially issued in a private placement, which closed on August 2, 2017. We are not selling any shares of common stock under this prospectus and will not receive any of the proceeds from the sale of shares of common stock by the selling stockholders.

The selling stockholders may offer the shares from time to time as each selling stockholder may determine through public or private transactions or through other means described in the section entitled “Plan of Distribution” or a supplement to this prospectus. Each selling stockholder may also sell shares under Rule 144 under the Securities Act of 1933, as amended, if available, rather than under this prospectus.

We are registering the offer and sale of these shares pursuant to certain registration rights granted to the selling stockholders. The registration of these shares of common stock does not necessarily mean that any of the shares will be offered or sold by the selling stockholders. The timing and amount of any sale is within the sole discretion of each selling stockholder.

The selling stockholders will pay all underwriting discounts and selling commissions, if any, in connection with the sale of the shares of common stock. We have agreed to pay certain expenses in connection with this registration statement and to indemnify the selling stockholders against certain liabilities. To our knowledge, as of the date of this prospectus, no underwriter or other person has been engaged to facilitate the sale of shares of common stock in this offering.

Our common stock is listed on The NASDAQ Global Market under the symbol “PRTO.” On August 11, 2017, the closing price of our common stock was \$1.30 per share.

***Investing in our common stock involves a high degree of risk. You should carefully read the risks and uncertainties included herein under the heading “Risk Factors” on page 7 of this prospectus, and under similar headings in our Annual Report on Form 10-K for the fiscal year ended December 31, 2016 and our Quarterly Reports on Form 10-Q for the quarterly periods ended March 31, 2017, which have been filed with the Securities and Exchange Commission, or the SEC, and are incorporated by reference in this prospectus and in the other documents that are filed after the date hereof and incorporated by reference into this prospectus.***

**Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.**

The date of this prospectus is \_\_\_\_\_, 2017.

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## ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3 that we filed with the U.S. Securities and Exchange Commission (the “SEC”), using a “shelf” registration process. By using such registration statement, the selling stockholders identified herein may, from time to time, offer and sell (in one or more transactions as described under “Plan of Distribution”) up to 22,112,775 shares of our common stock underlying our Series A Convertible Preferred Stock issued in our private placement offering which closed on August 2, 2017. We will not receive any of the proceeds from the sales of the common stock by the selling stockholders.

This prospectus provides you with a general description of us and our securities. We may add, update or change in a prospectus supplement any of the information contained in this prospectus or the documents incorporated by reference. For further information about our business and our securities, you should refer to the registration statement and the reports incorporated by reference in this prospectus, as described in “Additional Information” and “Incorporation of Certain Information by Reference”.

You must not rely upon any information or representation not contained or incorporated by reference in this prospectus. You should rely only on the information contained in this prospectus and in any prospectus supplement (including in any documents incorporated by reference herein or therein). You should not assume that the information contained in this prospectus is accurate on any date subsequent to the date set forth on the front of the document or that any information we have incorporated by reference is correct on any date subsequent to the date of the document incorporated by reference, even though this prospectus is delivered or securities are sold on a later date. We and the selling stockholders have not authorized anyone to provide you with any different information. The selling stockholders are offering to sell our securities, and seeking offers to buy, only in jurisdictions where offers and sales are permitted.

Proteon Therapeutics, Inc. is referred to herein as “Proteon”, “the Company”, “we”, “us”, and “our”, unless otherwise specified or the context indicates otherwise.

## PROSPECTUS SUMMARY

*This summary highlights selected information appearing elsewhere or incorporated by reference into this prospectus and may not contain all of the information that you need to consider in making your investment decision. You should read this prospectus, the applicable prospectus supplement and any related free writing prospectus that we have authorized for use in connection with this offering carefully, including the risks and uncertainties included herein under the heading "Risk Factors" beginning on page 7 in this prospectus and incorporated by reference from our most recent Annual Report on Form 10-K and our most recent Quarterly Report on Form 10-Q, before making an investment decision.*

### **About Us**

We are a late-stage biopharmaceutical company focused on the development of novel, first-in-class pharmaceuticals to address the medical needs of patients with kidney and vascular disease. Our product candidate, vonapanitase, is a recombinant human elastase that we are developing to improve vascular access outcomes in patients with chronic kidney disease, or CKD, 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 and Phase 3 clinical trials of vonapanitase in patients undergoing creation of an arteriovenous fistula support that a one-time, local application of vonapanitase during surgical creation of a radiocephalic fistula for hemodialysis may improve secondary patency (time to fistula abandonment) and fistula use for hemodialysis, thereby improving patient outcomes and reducing the burden on patients and the healthcare system. We are currently conducting our second Phase 3 trial, PATENCY-2, which is evaluating vonapanitase in radiocephalic fistulas, our initial indication. Following our review of the complete data sets from our first Phase 3 trial, PATENCY-1, and discussions with the U.S. Food and Drug Administration, or FDA, we amended the protocol for the PATENCY-2 trial in the first quarter of 2017. The protocol amendment reordered the existing endpoints for this ongoing trial, establishing secondary patency (time to fistula abandonment) and fistula use for hemodialysis as co-primary endpoints. The protocol amendment also increased the planned enrollment for this trial from 300 to 500 patients which we subsequently increased to 600 patients in the second quarter of 2017. The increased sample size of 600 patients for the PATENCY-2 trial provides power to detect the differences observed in the PATENCY-1 trial, with a p-value  $\leq 0.05$ , for secondary patency (time to fistula abandonment) and fistula use for hemodialysis of 88% and 98%, respectively. We received written confirmation from the FDA that, if PATENCY-2 is successful in showing statistical significance ( $p \leq 0.05$ ) on each of the co-primary endpoints, the PATENCY-2 trial together with data from previously completed studies would provide the basis for a Biologics License Application, or BLA, submission as a single pivotal study, in which case no additional studies would need to be conducted. Vonapanitase also received a Breakthrough Therapy designation from the FDA in May 2017 for hemodialysis vascular access. The FDA awards Breakthrough Therapy designations to expedite the development and review of investigational drugs that are intended to treat serious or life-threatening conditions when preliminary clinical evidence indicates that the treatment may offer a substantial improvement over currently available therapies on one or more clinically significant endpoints. We expect to complete enrollment for the PATENCY-2 trial in the first quarter of 2018 and to report top-line data in the first quarter of 2019. If the PATENCY-2 trial is successful, we expect to submit a BLA in 2019.

We commenced business operations in June 2001 and incorporated in March 2006. Our operations to date have been limited to organizing and staffing our company, business planning, raising capital, undertaking preclinical studies and clinical trials of vonapanitase, 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 our initial public offering, or IPO, completed in October 2014.

As of March 31, 2017, we had received an aggregate of \$174.5 million in net proceeds comprised of \$94.0 million from the issuance of private equity securities, \$7.7 million from the issuance of convertible notes, \$10.0 million from business development activities, \$0.2 million from government grants, \$62.5 million from our IPO and \$0.1 million from the sale of common stock under our at-the-market, or ATM, program with Cowen and Company, LLC.

We have never been profitable and have incurred net losses in each year since inception. As of March 31, 2017, we had an accumulated deficit of \$166.3 million and our net loss for the three months ended March 31, 2017 was \$6.5 million. 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, vonapanitase. If we obtain regulatory approval for vonapanitase, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. Furthermore, 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.

Prior to the sale of our Series A Convertible Preferred Stock, we believed that our cash and cash equivalents and available-for-sale investments as of March 31, 2017 would be sufficient to fund our operating expenses and capital expenditure requirements into the third quarter of 2018. We closed our \$22 million Series A Convertible Preferred Stock transaction on August 2, 2017 and, when including net proceeds from the sale of our Series A Convertible Preferred Stock along with our cash and cash equivalents and available-for-sale investments as of March 31, 2017, we believe we will have sufficient funds to cover our operating expenses and capital expenditure requirements into the fourth quarter of 2019, thus allowing us to complete enrollment of patients in our second Phase 3 trial of vonapanitase in radiocephalic fistulas, to fund our chemistry, manufacturing and controls, or CMC, activities and to obtain results from our second Phase 3 trial.

We do not expect to generate revenue from product sales unless and until we successfully complete development and obtain regulatory approval for vonapanitase, 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 vonapanitase, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. Accordingly, we may seek to further 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 additional 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 vonapanitase or any additional product candidates, if developed.

## **Recent Events**

### ***Private Placement***

On June 22, 2017, we entered into a securities purchase agreement (the "Purchase Agreement") with a syndicate of current and new institutional investors (each individually, an "Investor" and, collectively, the "Investors"), led by a fund affiliated with Deerfield Management Company, L.P. ("Deerfield"), pursuant to which we agreed to issue and sell to the Investors an aggregate of 22,000 shares (the "Preferred Shares") of the Company's Series A Convertible Preferred Stock, par value \$0.001 per share (the "Series A Preferred Stock" and such sale of the Series A Preferred Stock, the "Transaction"), for a purchase price of \$1,000 per share, or an aggregate purchase price of \$22.0 million, all upon the terms and conditions set forth in the Purchase Agreement. In the Purchase Agreement, we made customary representations and warranties to the Investors relating to the Company, our business and the issuance of the securities at the closing. The representations and warranties of the respective parties to the Purchase Agreement will survive the closing of the Transaction. Consummation of the Transaction was subject to customary closing conditions, including (i) approval by the Company's stockholders and (ii) minimum gross proceeds received by the Company from the sale of the Preferred Shares to all Investors at the closing of the Transaction equal to no less than \$18,000,000. We also agreed to indemnify the Investors for certain breaches of our representations and warranties in certain circumstances. We received stockholder approval for the Transaction on July 31, 2017 at a special meeting of our stockholders and the Transaction closed on August 2, 2017.

The following holders, or affiliates of holders, of more than 5% of our Common Stock have executed the Purchase Agreement as investors: Abingworth Bioventures VI, LP, a fund affiliated with Deerfield Management Company, L.P., Intersouth Partners VI, L.P., Pharmstandard International S.A., Skyline Venture Partners Qualified Purchaser Fund IV, LP, RA Capital and related funds, and TVM Capital and related funds. Additional information regarding ownership is described below in "Selling Stockholders."

In connection with the Transaction, concurrently with the execution and delivery of the Purchase Agreement, and as an inducement to the Investors to enter into the Purchase Agreement, the Company and certain stockholders of the Company entered into a Fifth Amended and Restated Investors' Rights Agreement, dated as of June 22, 2017 (the "Fifth IRA"), pursuant to which such stockholders agreed to certain limitations on the registration rights provided for under that certain Fourth Amended and Restated Investors' Rights Agreement, dated as of May 13, 2014. The Fifth IRA became effective upon the closing of the Transaction.

The rights, preferences and privileges of the Series A Preferred Stock are set forth in the Certificate of Designation of Preferences, Rights and Limitations of Series A Convertible Preferred Stock ("Certificate of Designation"), which we filed with the Secretary of State of the State of Delaware on August 1, 2017. Each share of Series A Preferred Stock is convertible into approximately 1,005 shares of our common stock, at a conversion price of \$0.9949 per share, in each case subject to adjustment for any stock splits, stock dividends and similar events, at any time at the option of the holder, provided that any conversion of Series A Preferred Stock by a holder into shares of Common Stock would be prohibited if, as a result of such conversion, the holder, together with its affiliates and any other person or entity whose beneficial ownership of our common stock would be aggregated with such holder's for purposes of Section 13(d) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), would beneficially own more than 9.985% of the total number of shares of our common stock issued and outstanding after giving effect to such conversion (the "Blocker"). For purposes of clarity, the shares of common stock underlying any holder's shares of Series A Preferred Stock in excess of the Blocker shall not be deemed to be beneficially owned by such holder for any purpose, including for purposes of Section 13(d) or Rule 16a-1(a)(1) of the Exchange Act. The Blocker may not be waived and shall apply to any successor holder of shares of Series A Preferred Stock.

For purposes of the Blocker, the aggregate number of shares of common stock beneficially owned by a holder and its Attribution Parties (as defined below) shall include the number of shares of common stock held by such holder and its Attribution Parties plus the number of shares of common stock issuable upon conversion of such shares of Series A Preferred Stock with respect to which the determination is being made, but shall exclude shares of common stock which would be issuable upon (i) conversion of the remaining, unconverted portion of the shares of Series A Preferred Stock beneficially owned by such holder or any of its Attribution Parties and (ii) exercise or conversion of the unexercised or unconverted portion of any other securities of the Company beneficially owned by such holder or any of its Attribution Parties, subject to certain limitations on conversion or exercise. For purposes of the Blocker, in determining the number of outstanding shares of common stock, a holder may rely on the number of outstanding shares as reflected in (1) the Company's most recent quarterly report on Form 10-Q or annual report on Form 10-K, as the case may be, (2) a more recent public announcement by the Company or (3) any other notice by the Company or the transfer agent for the common stock setting forth the number of shares of common stock outstanding.

The following defined terms are set forth in the Certificate of Designation:

“Attribution Parties” means, with respect to any holder, collectively, any of such Holder’s Affiliates (as defined below), any Persons (as defined below) acting as a “group” together with such Holder with respect to the common stock for purposes of Section 13(d) of the Exchange Act, and any other Persons whose beneficial ownership of the common stock would be aggregated with such Holder’s for purposes of Section 13(d) of the Exchange Act.

“Affiliate” means any Person (as hereinafter defined) that, directly or indirectly through one or more intermediaries, controls or is controlled by or is under common control with such Person, as such terms are used in and construed under Rule 144 under the Securities Act (“Rule 144”). With respect to a Holder, any investment fund or managed account that is managed on a discretionary basis by the same investment manager as such Holder will be deemed to be an Affiliate of such Holder. As used in this definition of “Affiliate,” the term “control” means the possession, directly or indirectly, of the power to direct or cause the direction of the management and policies of a Person, whether through ownership of voting securities or partnership or other ownership interest, by contract, or otherwise.

“Person” means an individual, a limited liability company, a partnership, a joint venture, a corporation, a trust, an unincorporated organization or a government or any department or agency thereof or any other legal entity.

In the event that the issuance of shares of common stock to any holder upon the conversion of any of such holder’s shares of Series A Preferred Stock results in such holder and its Attribution Parties being deemed to beneficially own, in the aggregate, a number of shares of common stock that exceeds the Blocker, the issuance of that number of shares so issued in excess of the Blocker (the “Excess Shares”), and the conversion of shares of Series A Preferred Stock resulting in such issuance, shall be deemed null and void and shall be cancelled ab initio, such holder shall not have the power to vote or to transfer the Excess Shares, and the shares of Series A Preferred Stock as to which the conversion was voided shall remain outstanding and continue to be held by such holder. As soon as reasonably practicable after such issuance and conversion have been deemed null and void, the Company shall return to such holder certificates representing the number of shares of Series A Preferred Stock corresponding to the voided issuance and conversion (to the extent such shares of Series A Preferred Stock were surrendered to the Company).

Prior to the first date (the “Preference Termination Date”) that the volume-weighted average price per share of common stock for each of the trading days during any twenty consecutive trading days ending on or at any time after the one year anniversary of the approval of the Company’s biologics license application for the Company’s product vonapanitase by the United States Food and Drug Administration is greater than 200% of the conversion price, the holders of a majority of the outstanding shares of Series A Preferred Stock will be entitled to elect one (1) member of the Board (the “Series A Director”). On August 2, 2017, the holders of a majority of the outstanding shares of Series A Preferred Stock elected Jonathan Leff to serve as the Series A Director. Mr. Leff is a Partner at Deerfield Management Company, L.P., the investment manager of Deerfield Private Design Fund IV, L.P., serving on the Private Transactions team and as Chairman of the Deerfield Institute.

The Series A Director is entitled to the same compensation, the same indemnification and the same director and officer insurance in connection with such Series A Director’s service as a director as all other non-employee members of the Board, and the Series A Director is entitled to reimbursement for documented, reasonable out-of-pocket expenses incurred in attending meetings of the Board and any committees thereof, to the same extent as all other non-employee members of the Board. In addition, the Series A Director is entitled to the same information regarding the Company and its subsidiaries in connection with the Series A Director’s service as a director as all other members of the Board. Further, the Series A Director will hold office until the following year’s annual meeting of the Company’s stockholders and until his or her successor is duly elected or qualified by the written consent of the holders of a majority of the outstanding shares of Series A Preferred Stock or until his or her earlier death, incapacity, resignation or removal. Such Series A Director may be removed from office, with or without cause, upon the written consent of the holders of a majority of the outstanding shares of Series A Preferred Stock, and the holders of a majority of the outstanding shares of Series A Preferred Stock shall have the power to fill, by written consent, any vacancy caused by the resignation, death or removal of such Series A Director. For purposes of clarity, the Series A Director shall not be classified with the remaining members of the Board of Directors.

Contemporaneously with the closing of the Transaction, we entered into a Registration Rights Agreement with the Investors (the “Registration Rights Agreement”). Pursuant to the Registration Rights Agreement, the Investors are entitled to certain shelf and “piggyback” registration rights with respect to the Conversion Shares, subject to the limitations set forth in the Registration Rights Agreement. In addition, pursuant to the Registration Rights Agreement, we agreed to file a registration statement on Form S-3 with the SEC, within 20 days after the closing of the Transaction, to register for resale the Conversion Shares that are issuable upon the conversion of the Preferred Shares issued at closing, and any additional shares of common stock as may become issuable with respect to such securities as a result of stock splits, stock dividends or similar transactions (the “Registrable Securities”), and to maintain the effectiveness of such registration statement(s) until all the shares of common stock have been sold in accordance with the Registration Statement or in accordance with Rule 144 under the Securities Act or may be sold by the selling stockholder without volume or manner-of-sale restrictions, and without compliance with any “current public information” requirement, pursuant to Rule 144 under the Securities Act. We filed this registration statement to comply with our requirements under the Registration Rights Agreement.



If, at any time prior to the date that no investors hold Registrable Securities, the Company (i) files with the SEC a registration statement under the Securities Act relating to an offering for its own account or for the account of any other holder of its equity securities (other than securities being registered on Form S-4 or Form S-8), and/or (ii) otherwise effects an underwritten offering of any securities of the Company of a type included in a then effective registration statement, then, subject to certain limitations, we are required to send each Investor written notice of such action and include in such registration statement and/or underwritten offering all or any part of such investor's Registrable Securities that the investor requests, or the underwriters allow, to be included in such registration statement and/or the underwritten offering.

If the Company fails to comply with specified provisions in the Registration Rights Agreement, including if a registration statement is not filed with the SEC as required by the Registration Rights Agreement, then we will agree to pay each investor, in addition to all other available remedies, damages, for each 30-day period after the date of such failure until it is cured, an amount in cash equal to one and one-half percent (1.5%) of the product of (i) the sum of (x) the aggregate number of Conversion Shares that are then issued and issuable upon conversion of the Preferred Shares that constitute Registrable Securities and are included, or to be included, as applicable, in the registration statement, as of the date such registration failure occurs (without regard to any limitations on conversion or issuance set forth in the Certificate of Designation), plus (y) all other shares of common stock that constitute Registrable Securities and are included, or to be included, as applicable, in such Registration Statement, as of the date such registration failure occurs, multiplied by (ii) the volume weighted average price of the common stock on such date.

### **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 (i) the beginning of the first fiscal year following the fifth anniversary of our initial public offering, (ii) the beginning of the first fiscal year after our annual gross revenue is \$1.07 billion or more, (iii) the date on which we have, during the previous three-year period, issued more than \$1.0 billion in non-convertible debt securities and (iv) as of the end of any fiscal year in which the market value of our common stock held by non-affiliates exceeded \$700 million as of the end of the second quarter of that fiscal year.

For as long as we remain an "emerging growth company," we may take advantage of certain exemptions from various reporting requirements that are applicable to public companies that are not "emerging growth companies" including, but not limited to, not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation and financial statements in our periodic reports and proxy statements, and exemptions from the requirements of holding a nonbinding advisory vote to approve executive compensation and shareholder approval of any golden parachute payments not previously approved. We plan to take advantage of these reporting exemptions until we are no longer an "emerging growth company."

### **Corporate Information**

We were incorporated in Delaware in March 2006, and at that time, acquired Proteon Therapeutics, LLC, our predecessor, which was formed in June 2001. Our principal 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 in, or that can be accessed through, our website is not part of this prospectus.

## THE OFFERING

Common Stock Offered by Selling Stockholders:	22,112,775 shares
Use of Proceeds:	We will not receive any of the proceeds from the sale of any of our shares by the selling stockholders.
Risk Factors:	Investing in our common stock involves risks. Please refer to the sections titled "Risk Factors" beginning on page 7 of this prospectus, as well as the risks and uncertainties discussed under the section titled "Risk Factors" in our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q or Current Reports on Form 8-K; "Cautionary Note Regarding Forward-Looking Statements" on page 9 of this prospectus, and other information included or incorporated by reference in this prospectus supplement and the accompanying prospectus for a discussion of factors you should carefully consider before investing our securities.
NASDAQ Global Market Symbol:	PRTO

Unless otherwise stated, all information in this prospectus assumes no conversion of the Series A Preferred Stock, no exercise of outstanding options or warrants to purchase common stock and no issuance of shares available for future issuance under our equity compensation plans.

## RISK FACTORS

An investment in our securities involves a high degree of risk. Before making an investment decision, you should carefully consider the risks described below and under “Risk Factors” in the applicable prospectus supplement and in our most recent Annual Report on Form 10-K, and in our updates to those Risk Factors in our Quarterly Reports on Form 10-Q or Current Reports on Form 8-K following the most recent Form 10-K, and in all other information appearing in this prospectus or incorporated by reference into this prospectus and any applicable prospectus supplement. The material risks and uncertainties that management believes affect us will be described in those documents. In addition to those risk factors, there may be additional risks and uncertainties of which management is not aware or focused on or that management deems immaterial. Our business, financial condition or results of operations could be materially adversely affected by any of these risks. The trading price of our securities could decline due to any of these risks, and you may lose all or part of your investment. This prospectus is qualified in its entirety by these risk factors.

### **Additional Risks Relating to This Offering and Our Common Stock**

**The sale of a substantial amount of our common stock, including resale of the shares of common stock issuable upon the conversion of the Series A Preferred Stock acquired in the Transaction, in the public market after this offering could adversely affect the prevailing market price of our common stock and cause stockholders to experience dilution.**

We have outstanding an aggregate of 17,619,418 shares of our common stock as of August 11, 2017. We have received stockholder approval for the Transaction and, therefore, the outstanding shares of Series A Preferred Stock are convertible into our common stock at each Investor’s election, subject to the Blocker. The Series A Preferred Stock is convertible into an aggregate of 22,112,775 shares of common stock, subject to adjustment as provided in the Certificate of Designation. Pursuant to the registration rights granted in the Transaction, we agreed to register the resale by the selling stockholders named herein of these shares of common stock. Upon such registration, these shares will become generally available for immediate resale, subject to the Blocker. Sales of substantial amounts of shares of our common stock in the public market, or the perception that such sales might occur, could adversely affect the market price of our common stock, and the market value of our other securities, and could result in substantial dilution to shareholders who held our common stock prior to the Transaction. In addition, we may issue additional shares of common stock or other equity or debt securities convertible into common stock in connection with a future financing, acquisition, litigation settlement, employee arrangements or otherwise. Any such issuance could result in substantial dilution to our existing stockholders and could cause our stock price to decline.

A substantial number of shares of common stock are being offered by this prospectus, and we cannot predict if and when the purchasers may sell such shares in the public markets. In addition, certain holders of our common shares have additional rights, subject to some conditions, to require us to file registration statements covering the sale of their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. We have also registered the offer and sale of all shares of common stock that we may issue under our equity compensation plans. Furthermore, in the future, we may issue additional shares of common stock or other equity or debt securities convertible into common stock in connection with a financing, acquisition, litigation settlement, employee arrangements or otherwise. Any such issuance could result in substantial dilution to our existing stockholders and could cause our stock price to decline.

**Our share price may be volatile, which could subject us to securities class action litigation and our stockholders could incur substantial losses.**

The market price of shares of our common stock could be subject to wide fluctuations in response to many risk factors listed in this section, and others beyond our control, including:

- actual or anticipated fluctuations in our financial condition and operating results;
- actual or anticipated changes in our growth rate relative to our competitors;
- failure to meet or exceed financial estimates and projections of the investment community or that we provide to the public;
- failure to meet or exceed financial estimates and projections of the investment community or that we provide to the public;
- issuance of new or updated research or reports by securities analysts;
- fluctuations in the valuation of companies perceived by investors to be comparable to us;
- additions or departures of key management or other personnel;
- disputes or other developments related to proprietary rights, including patents, litigation matters, and our ability to obtain patent protection for our technologies;
- disputes or other developments related to proprietary rights, including patents, litigation matters, and our ability to obtain patent protection for our technologies;
- announcement or expectation of additional debt or equity financing efforts;
- sales of our common stock by us, our insiders or our other stockholders; and
- general economic and market conditions.

These and other market and industry factors may cause the market price and demand for our common stock to fluctuate substantially, regardless of our actual operating performance, which may limit or prevent investors from readily selling their shares of common stock and may otherwise negatively affect the liquidity of our common stock. In addition, the stock market in general, and NASDAQ and emerging growth companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. In the past, when the market price of a stock has been volatile, holders of that stock have instituted securities class action litigation against the company that issued the stock. If in the future any of our stockholders brought a lawsuit against us, we could incur significant legal expenses, settlement costs or damage awards that are not covered by, or exceed the limits of, our available directors’ and officers’ liability insurance, which could adversely impact our financial condition, results of operations or cash flows. Such a lawsuit could also divert the time and attention of our management.

## CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus and each prospectus supplement, including the documents that we incorporate by reference, contains or may contain forward-looking statements as that term is defined in the federal securities laws. The events described in forward-looking statements contained in this prospectus, including the documents that we incorporate by reference, may not occur. Generally, these statements relate to our business plans or strategies, projected or anticipated benefits or other consequences of our plans or strategies, financing plans, projected or anticipated benefits from acquisitions that we may make, or projections involving anticipated revenues, earnings or other aspects of our operating results or financial position, and the outcome of any contingencies. Any such forward-looking statements are based on current expectations, estimates and projections of management. We intend for these forward-looking statements to be covered by the safe-harbor provisions for forward-looking statements. Words such as “may,” “expect,” “believe,” “anticipate,” “project,” “plan,” “intend,” “estimate,” and “continue,” and their opposites and similar expressions are intended to identify forward-looking statements. We caution you that these statements are not guarantees of future performance or events and are subject to a number of uncertainties, risks and other influences.

These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including, but not limited to:

- the timing of completing enrollment or releasing data or results of our ongoing and planned clinical trials for vonapanitase (formerly PRT-201);
- our estimates regarding the amount of funds we require to complete our Phase 3 clinical trial for vonapanitase;
- our interpretation of the data from our completed Phase 2 and Phase 3 clinical trials for vonapanitase;
- whether and when we may submit a Biologics License Application or a supplemental Biologics License Application;
- whether we will need to conduct any additional studies after our Phase 3 trials;
- our estimates regarding the amount of funds required to fund operations into the fourth quarter of 2019;
- our plans to fund our chemistry, manufacturing and controls;
- our estimates regarding expenses, future revenues, capital requirements, the sufficiency of our current and expected cash resources and our need for additional financing and plans for additional financing;
- our estimate of when we will require additional funding;
- our plans to commercialize and bring vonapanitase to market;
- the timing of, and our ability to obtain and maintain, regulatory approvals for our product candidates, including vonapanitase;
- the rate and degree of market acceptance and clinical utility of any approved product candidate and the general market for the prevention of vascular access failure;
- our ability to quickly and efficiently identify and develop additional product candidates;
- our search for additional product opportunities;
- our commercialization, marketing, distribution and manufacturing capabilities, strategy and expenses;
- plans to initiate or continue Phase 1 or Phase 1/2 trials in symptomatic peripheral artery disease or other indications; and
- our plans to improve existing, and implement new, systems to manage our business.

You should also consider carefully the statements set forth in the section titled “Risk Factors” or elsewhere in this prospectus and the documents incorporated or deemed incorporated herein by reference, including but not limited to the risks described in under “Risk Factors” and elsewhere in our most recent Annual Report on Form 10-K and in our updates to those risk factors in our Quarterly Reports on Form 10-Q and Current Reports on Form 8-K and other factors described elsewhere in this prospectus. Any one or more of these uncertainties, risks and other influences could materially affect our results of operations and whether forward-looking statements made by us ultimately prove to be accurate. Our actual results, performance and achievements could differ materially from those expressed or implied in these forward-looking statements. Except as otherwise required by law, we undertake no obligation to publicly update or revise any forward-looking statements, whether from new information, future events or otherwise.

## USE OF PROCEEDS

We will not receive any proceeds from the sale of our common stock by the selling stockholders.

The selling stockholders will pay any underwriting discounts and commissions and any similar expenses it incurs in disposing of the common stock. We will bear all other reasonable costs, fees and expenses incurred in effecting the registration of the common stock covered by this prospectus, including all registration and filing fees, fees and expenses of compliance with securities or "blue sky" laws, listing application fees, printing expenses, transfer agent's and registrar's fees, costs of distributing prospectuses in preliminary and final form as well as any supplements thereto, and fees and disbursements of counsel for the Company and all independent certified public accountants and other persons retained by the Company.

## SELLING STOCKHOLDERS

As described in the prospectus summary, in the Transaction, the selling stockholders acquired shares of our Series A Preferred Stock that are convertible into shares of our common stock, subject to the limitations described below. In connection with the closing of the Transaction, we entered into the Registration Rights Agreement, pursuant to which we agreed to prepare and file one or more registration statements covering the resale of the shares of common stock issuable upon the conversion of the Series A Preferred Stock acquired in the Transaction (without regard to the limitation described below), and to maintain the effectiveness of such registration statement(s) until all the shares of common stock have been sold in accordance with the Registration Statement or in accordance with Rule 144 under the Securities Act or may be sold by the selling stockholder without volume or manner-of-sale restrictions, and without compliance with any “current public information” requirement, pursuant to Rule 144 under the Securities Act. We are filing this registration statement to comply with our requirements under the Registration Rights Agreement.

Under the terms of the Series A Preferred Stock, any conversion of Series A Preferred Stock by a holder into shares of common stock will be prohibited to the extent that, as a result of such conversion, the holder, together with its affiliates and any other person or entity whose beneficial ownership of common stock would be aggregated with such holder’s for purposes of Section 13(d) of the Securities and Exchange Act of 1934, as amended, would beneficially own more than 9.985% of the total number of shares of common stock issued and outstanding after giving effect to such conversion (the “Blocker”). The Blocker may not be waived and shall apply to any successor holder of shares of Series A Preferred Stock. The table below does not reflect such limitation, with the effect that beneficial ownership of the selling stockholders is calculated and presented (for purposes of disclosure in this prospectus only) on a fully as converted basis. This table is based upon information supplied by the selling stockholders.

The following table sets forth information as of August 11, 2017, and includes the shares of our common stock beneficially owned by each of the selling stockholders (as well as certain shares of Common Stock that, as a result of the Blocker, the selling stockholders may not currently have the right to acquire), the shares of common stock being registered for sale and offered for sale by each of the selling stockholders, and the shares of common stock that will be beneficially owned by each of the selling stockholders upon sale of the shares registered for resale, assuming that such selling stockholder sells all shares of common stock potentially issuable upon conversion of the Series A Preferred Stock acquired by such selling stockholder in the Transaction. The percentage of shares owned in the table below is based on 39,732,193 shares of common stock outstanding, which includes 17,619,418 shares of common stock outstanding as of August 11, 2017 and assumes the sale of 22,112,775 shares of common stock potentially issuable upon conversion of the Series A Preferred Stock as of the date of this prospectus. Only those selling stockholders listed below or their transferees, pledgees, donees, assignees, distributees or successors in interest may offer and sell the common stock pursuant to this prospectus and any accompanying prospectus supplement. The selling stockholders may offer all or less than all of the shares listed in the table below for sale pursuant to this prospectus and any accompanying prospectus supplement from time to time. Accordingly, no estimate can be given as to the shares of common stock that the selling stockholders will hold upon consummation of any such sales. Beneficial ownership is determined in accordance with the rules of the SEC, except that the following table does not reflect the limitations of the Blocker described above, with the effect that beneficial ownership of the selling stockholders is calculated and presented (for purposes of disclosure in this prospectus only) on a fully as converted basis.

Name of Selling Stockholder	Beneficial Ownership Prior to the Offering	Maximum Number of Shares Being Offered (10)	Beneficial Ownership After the Offering	
			Number	Percent
Deerfield Private Design Fund IV, L.P. (1)	16,082,018	16,082,018	--	--
Abingworth Bioventures VI, LP. (2)	4,583,485	2,538,949	2,044,536	5.1%
Skyline Venture Partners Qualified Purchaser Fund IV, L.P. (3)	2,492,333	1,059,403	1,432,930	3.6%
TVM Life Science Ventures VI GmbH & Co. KG (4)	2,445,622	373,907	1,943,059	4.9%
TVM Life Science Ventures VI LP (4)	2,445,622	128,656	1,943,059	4.9%
Pharmstandard International S.A. (5)	1,667,907	502,563	1,165,344	2.9%
Intersouth Partners VI, L.P. (6)	1,300,433	402,050	898,383	2.3%

RA Capital Healthcare Fund, L.P. (7)	1,354,737	275,405	1,079,332	2.7%
Blackwell Partners LLC – Series A (7)	324,468	66,338	258,130	0.7%
Perceptive Life Sciences Master Fund LTD (8)	675,859	341,743	334,116	0.8%
Fairmount Healthcare Fund, L.P. (9)	449,745	341,743	108,002	0.3%

- (1) Deerfield Mgmt IV, L.P. is the general partner of Deerfield Private Design Fund IV, L.P. Deerfield Management Company, L.P. is the investment manager of Deerfield Private Design Fund IV, L.P. Mr. James E. Flynn is the sole member of the general partner of Deerfield Mgmt IV, L.P. and Deerfield Management Company, L.P. Each of Deerfield Mgmt IV, L.P., Deerfield Management Company, L.P. and Mr. Flynn may be deemed to beneficially own the shares beneficially owned by Deerfield Private Design Fund IV, L.P. Deerfield Management Company, L.P. and Mr. Flynn beneficially own, through affiliated funds, an additional aggregate of 1,224,899 shares of common stock representing approximately 6.95% of our outstanding shares of common stock.
- (2) Abingworth LLP and Abingworth Bioventures VI LP (“ABV VI”) may be deemed to have shared voting power and shared dispositive power with respect to (i) 2,017,872 shares of our common stock held by ABV VI, (ii) 26,664 shares of our common stock issuable upon exercise of options issued to Tim Haines, our director, and (iii) up to 2,538,949 shares of our common stock being offered pursuant to this prospectus by ABV VI, which are potentially issuable upon conversion of 2,526 shares of Series A Preferred Stock held by ABV VI, depending on, among other factors, the number of shares of our common stock outstanding from time to time. Abingworth Bioventures VI GP LP, a Scottish limited partnership, serves as the general partner of 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 Stephen W. Bunting, Kurt von Emster, Genghis Lloyd-Harris, and Tim 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 LLP, Abingworth Bioventures VI GP LP, Abingworth General Partner VI LLP, Stephen W. Bunting, Kurt von Emster, Genghis Lloyd-Harris, and Tim Haines disclaims beneficial ownership of the securities held by ABV VI except to the extent of their proportionate pecuniary interest therein.
- (3) Skyline Venture Management IV, LLC (“SVM IV”), John G. Freund, M.D., our director, and Yasunori Kaneko may be deemed to have shared voting power and shared dispositive power with respect to up to 2,492,333 shares of our common stock held by Skyline Venture Partners Qualified Purchaser Fund IV, L.P. (“SVP IV”), including 1,059,403 shares of common stock being offered pursuant to this prospectus by SVP IV, which are potentially issuable upon conversion of 1,054 shares of Series A Preferred Stock held by SVP IV, depending on, among other factors, the number of shares of our common stock outstanding from time to time. SVM IV is the sole general partner of SVP IV. Each of John G. Freund, M.D., and Yasunori Kaneko are managing directors of SVM IV. Each of SVM IV, John G. Freund, M.D. and Yasunori Kaneko disclaims beneficial ownership of the shares held by SVP IV, except to the extent of their pecuniary interests therein.
- (4) TVM Life Science Ventures VI GmbH & Co. KG (“TVM VI German”), TVM Life Science Ventures VI LP (“TVM VI Cayman”), TVM Life Science Ventures Management VI L.P. (“TVM VI Management”), Helmut Schühlsler, Stefan Fischer and Hubert Birner, Ph.D., our director, may be deemed to have shared voting power and shared dispositive power with respect to up to 2,445,622 shares of our common stock, including 373,907 and 128,656 shares of our common stock being offered pursuant to this prospectus by TVM VI German and TVM VI Cayman, respectively, which are potentially issuable upon conversion of 372 and 128 shares of Series A Preferred Stock held by TVM VI German and TVM VI Cayman, respectively, depending on, among other factors, the number of shares of our common stock outstanding from time to time. Helmut Schühlsler, Stefan Fischer and Hubert Birner, Ph.D., our director, are members of the investment committee of TVM VI Management, the managing limited partner of TVM VI German and TVM VI Cayman with voting and dispositive power over the share held by those entities. TVM VI German, TVM VI Cayman, TVM VI Management and these individuals each disclaim beneficial ownership of such shares except to the extent of any pecuniary interest therein.
- (5) Pharmstandard International S.A. and the Joint Stock Company “Pharmstandard” may be deemed to have shared voting power and shared dispositive power with respect to 1,667,907 shares of our common stock held by Pharmstandard International S.A., including 502,563 shares of our common stock being offered pursuant to this prospectus by Pharmstandard International S.A., which are potentially issuable upon conversion of 500 shares of Series A Preferred Stock held by Pharmstandard International S.A., depending on, among other factors, the number of shares of our common stock outstanding from time to time. Pharmstandard International S.A. is a subsidiary of Joint Stock Company “Pharmstandard.” As the parent entity, JSC “Pharmstandard” may be deemed to have voting and investment control over the shares held by Pharmstandard International S.A. JSC “Pharmstandard” disclaims beneficial ownership of such shares except to the extent of any pecuniary interest therein.
- (6) Intersouth Associates VI, LLC (“ISA VI”), the general partner of Intersouth Partners VI, L.P. (“ISP VI”), Dennis J. Dougherty and Mitchell Mumma may be deemed to have shared voting and dispositive power with respect to 1,300,433 shares of our common stock held by ISP VI, including 402,050 shares of common stock being offered pursuant to this prospectus by ISP VI, which are potentially issuable upon conversion of 400 shares of Series A Preferred Stock held by ISP VI, depending on, among other factors, the number of shares of our common stock outstanding from time to time. Dennis J. Dougherty and Mitchell Mumma are the managing members of Intersouth Associates VI, LLC. Each of ISA VI, Dennis J. Dougherty and Mitchell Mumma disclaims beneficial ownership of such shares, except to the extent of any pecuniary interest therein.
- (7) RA Capital Healthcare Fund, L.P. (“RA Fund”) has shared voting power and shared dispositive power with respect to 1,354,737 shares of our Common Stock, including 275,405 shares of Common Stock issuable upon conversion of the Series A Preferred Stock. Dennis. RA Capital Management, LLC (“RA Capital”) has the shared voting power and shared dispositive power with respect to 1,679,205 shares of our Common Stock, including (a) 1,354,737 shares of our Common Stock held by RA Fund, for which RA Capital serves as the sole general partner, and which includes 275,405 shares of Common Stock issuable upon conversion of the Series A Preferred Stock, and (b) 324,468 shares of our Common Stock held in a separately managed account, Blackwell Partners LLC – Series A (“Blackwell”), for which RA Capital serves as investment adviser, and which includes 66,338 shares of Common Stock being offered pursuant to this prospectus. Peter Kolchinsky, Ph.D., as the manager of RA Capital, has the shared voting power and shared dispositive power with respect to 1,354,737 shares of our Common Stock held by RA Fund, and has the shared voting power and shared dispositive power with respect to 324,468 shares of our Common Stock held in a separately managed account for Blackwell. Each of RA Capital and Dr. Kolchinsky disclaims beneficial ownership for the shares, except to the extent of its or his pecuniary interest therein.





- (8) Perceptive Advisors LLC and Joseph Edelman had shared voting power and dispositive power over 675,859 shares of common stock held by Perceptive Life Sciences Master Fund Ltd (the “Fund”), including 341,743 shares of Common Stock being offered pursuant to this prospectus. Perceptive Advisors LLC serves as the investment manager to the Fund. Joseph Edelman is the managing member of Perceptive Advisors LLC.
- (9) Fairmount Funds Management LLC (“FFM”) (the investment manager of Fairmount Healthcare Fund L.P. (“FHF”)), Peter Harwin and Tomas Kiselak may be deemed to have shared voting and dispositive power with respect to 449,745 shares of our common stock held by FHF, including 341,743 shares of common stock being offered pursuant to this prospectus by FHF, which are potentially issuable upon conversion of 340 shares of Series A Preferred Stock held by FHF, depending on, among other factors, the number of shares of our common stock outstanding from time to time. Peter Harwin and Tomas Kiselak are the managing members of both FFM and Fairmount Healthcare Fund GP LLC (“FHF GP”). Each of FFM, FHF GP, Peter Harwin and Tomas Kiselak disclaims beneficial ownership of such shares, except to the extent of any pecuniary interest therein.
- (10) The maximum number of shares of common stock being registered for resale is based upon each share of Series A Preferred Stock being convertible into approximately 1,005 shares of our common stock, at a conversion price of \$0.9949 per share (subject to adjustment as set forth in the Certificate of Designation), and the applicable number of shares of Series A Preferred Stock purchased by each selling stockholder in the Transaction.

No offer or sale pursuant to this prospectus may occur unless the registration statement that includes this prospectus has been declared effective by the SEC and remains effective at the time a selling stockholder offers or sells shares of Common Stock. We are required, under certain circumstances, to update, supplement or amend this prospectus to reflect material developments in our business, financial position and results of operations and may do so by an amendment to this prospectus, a prospectus supplement or a future filing with the SEC incorporated by reference in this prospectus.

## PLAN OF DISTRIBUTION

Each selling stockholder of the securities named herein and any of their transferees, pledgees, donees, assignees, distributees or successors in interest (all of which may be selling stockholders) may, from time to time, sell any or all of their securities covered hereby on any stock exchange, market or trading facility on which the securities are traded, in private transactions or otherwise. These sales may be at fixed or negotiated prices or at market prices prevailing at the time of sale. A selling stockholder may use any one or more of the following methods when selling securities:

- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which the broker-dealer will attempt to sell the securities as agent but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker-dealer as principal and resale by the broker-dealer for its account;
- an exchange distribution in accordance with the rules of the applicable exchange;
- privately negotiated transactions;
- settlement of short sales;
- in transactions through broker-dealers that agree with the selling stockholders to sell a specified number of such securities at a stipulated price per security;
- through the writing or settlement of options or other hedging transactions, whether through an options exchange or otherwise;
- a combination of any such methods of sale; or
- any other method permitted pursuant to applicable law.

The selling stockholders may also sell securities under Rule 144 or any other exemption from registration under the Securities Act, if available, rather than under this prospectus.

Broker-dealers engaged by the selling stockholders may arrange for other brokers-dealers to participate in sales. Broker-dealers may receive commissions or discounts from the selling stockholders (or, if any broker-dealer acts as agent for the purchaser of securities, from the purchaser) in amounts to be negotiated, but, except as set forth in a supplement to this Prospectus, in the case of an agency transaction not in excess of a customary brokerage commission in compliance with FINRA Rule 2440; and in the case of a principal transaction a markup or markdown in compliance with FINRA IM-2440.

In connection with the sale of the securities or interests therein, the selling stockholders may enter into hedging transactions with broker-dealers or other financial institutions, which may in turn engage in short sales of the securities in the course of hedging the positions they assume. The selling stockholders may also sell securities short and deliver these securities to close out their short positions, or loan or pledge the securities to broker-dealers that in turn may sell these securities. The selling stockholders may also enter into option or other transactions with broker-dealers or other financial institutions or create one or more derivative securities which require the delivery to such broker-dealer or other financial institution of securities offered by this prospectus, which securities such broker-dealer or other financial institution may resell pursuant to this prospectus (as supplemented or amended to reflect such transaction).

The selling stockholders may pledge or grant a security interest in some of all of the shares of common stock owned by them and, if any of them defaults in the performance of its secured obligations, the pledgees or secured parties may offer and sell the shares of common stock from time to time pursuant to this prospectus or any supplement or amendment to this prospectus under Rule 424(b)(3) or other applicable provision of the Securities Act, amending, if necessary, the list of selling stockholders to include the pledgee, transferee or other successors in interest as selling stockholders under this prospectus. The selling stockholders also may transfer and donate the shares of common stock in other circumstances in which case the transferees, donees or other successors in interest will be the selling beneficial owners for purposes of this prospectus.

The selling stockholders and any broker-dealers or agents that are involved in selling the securities may be deemed to be “underwriters” within the meaning of the Securities Act in connection with such sales. In such event, any commissions received by such broker-dealers or agents and any profit on the resale of the securities purchased by them may be deemed to be underwriting commissions or discounts under the Securities Act. We are not aware that any selling stockholder has any written or oral agreement or understanding, directly or indirectly, with any person to distribute the securities.

We are required to pay certain fees and expenses incurred by us incident to the registration of the securities. We have agreed to indemnify the selling stockholders against certain losses, claims, damages and liabilities, including liabilities under the Securities Act.

We agreed to keep this prospectus effective until the earlier of (i) the date on which the securities may be resold by the selling stockholders without registration or restriction (including any volume or manner-of-sale limitations pursuant to Rule 144), without the requirement for us to be in compliance with the current public information requirement under Rule 144 under the Securities Act or any other rule of similar effect or (ii) all of the securities have been sold pursuant to this prospectus or Rule 144 under the Securities Act or any other rule of similar effect. The resale securities will be sold only through registered or licensed brokers or dealers if required under applicable state securities laws.

Under applicable rules and regulations under the Exchange Act, any person engaged in the distribution of the shares of common stock may not simultaneously engage in market making activities with respect to the common stock for the applicable restricted period, as defined in Regulation M, prior to the commencement of the distribution. In addition, the selling stockholders will be subject to applicable provisions of the Exchange Act and the rules and regulations thereunder, including Regulation M, which may limit the timing of purchases and sales of the common stock by the selling stockholders or any other person. We will make copies of this prospectus available to the selling stockholders.

## LEGAL MATTERS

The validity of the securities being offered hereby will be passed upon by Morgan, Lewis & Bockius LLP.

## EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2016, as set forth in their report, which is incorporated by reference in this prospectus and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

## DISCLOSURE OF COMMISSION POSITION ON INDEMNIFICATION FOR SECURITIES ACT LIABILITIES

Section 145 of the Delaware General Corporation Law, or DGCL, or Section 145, provides that we may indemnify 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 or investigative (other than an action by us or in our right) by reason of the fact that he is or was our director, officer, employee or agent, or is or was serving at our request as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, against expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by him or her in connection with such action, suit or proceeding if he acted in good faith and in a manner he or she reasonably believed to be in or not opposed to our best interests, and, with respect to any criminal action or proceeding, had no reasonable cause to believe his or her conduct was unlawful. Section 145 further provides that we similarly may indemnify any such person serving in any such capacity who was or is a party or is threatened to be made a party to any threatened, pending or completed action or suit by us or in our right to procure judgment in our favor, against expenses actually and reasonably incurred in connection with the defense or settlement of such action or suit if he or she acted in good faith and in a manner he reasonably believed to be in or not opposed to our best interests and except that no indemnification shall be made in respect of any claim, issue or matter as to which such person shall have been adjudged to be liable to us unless and only to the extent that the Delaware Court of Chancery or such other court in which such action or suit was brought shall determine upon application that, despite the adjudication of liability but in view of all the circumstances of the case, such person is fairly and reasonably entitled to indemnity for such expenses which the Delaware Court of Chancery or such other court shall deem proper.

Our amended and restated certificate of incorporation and bylaws provide that, to the fullest extent permitted by the DGCL, our directors shall not be liable to us or our stockholders for monetary damages for any breach of fiduciary duty as a director, and that we shall, to the maximum extent permitted under the DGCL, indemnify any person who was or is made a party or is threatened to be made a party to any threatened, pending or completed action, suit, proceeding or claim, whether civil, criminal, administrative or investigative, by reason of the fact that such person is or was or has agreed to be our director or officer or while a director or officer is or was serving at our request as a director, officer, partner, trustee, employee, or agent of any corporation, partnership, joint venture, trust or other enterprise, including service with respect to employee benefit plans, against expenses (including attorney's fees), judgments, fines, penalties and amounts paid in settlement incurred in connection with the investigation, preparation to defend or defense of such action, suit, proceeding or claim.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to our directors, officers and controlling persons pursuant to the foregoing provisions, or otherwise, we have been advised that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities 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, 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 such indemnification by us is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

## ADDITIONAL INFORMATION

This prospectus is part of a Registration Statement on Form S-3 that we have filed with the SEC relating to the shares of our securities being offered hereby. This prospectus does not contain all of the information in the Registration Statement and its exhibits. The Registration Statement, its exhibits and the documents incorporated by reference in this prospectus and their exhibits, all contain information that is material to the offering of the Securities hereby. Whenever a reference is made in this prospectus to any of our contracts or other documents, the reference may not be complete. You should refer to the exhibits that are a part of the Registration Statement in order to review a copy of the contract or documents. The Registration Statement and the exhibits are available at the SEC's Public Reference Room or through its Website.

We file annual, quarterly and current reports, proxy statements and other information with the SEC. You can read and copy any materials we file with the SEC at its Public Reference Room at 100 F Street, N.E., Washington, D.C. 20549 and at its regional offices, a list of which is available on the Internet at <http://www.sec.gov/contact/addresses.htm>. You may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. The SEC maintains an Internet site at <http://www.sec.gov> that contains reports, proxy and information statements, and other information regarding issuers, such as us, that file electronically with the SEC. Additionally, you may access our filings with the SEC through our website at <http://www.proteontherapeutics.com>. The information on our website is not part of this prospectus.

We will provide you without charge, upon your oral or written request, with a copy of any or all reports, proxy statements and other documents we file with the SEC, as well as any or all of the documents incorporated by reference in this prospectus or the registration statement (other than exhibits to such documents unless such exhibits are specifically incorporated by reference into such documents). Requests for such copies should be directed to:

Investor Relations  
Proteon Therapeutics, Inc.  
200 West Street  
Waltham, Massachusetts 02451  
Telephone number: (781) 890-0102

You should rely only on the information in this prospectus and the additional information described above and under the heading “Incorporation of Certain Information by Reference” below. We have not, and the selling stockholders have not, authorized any other person to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely upon it. The selling stockholders are not making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information in this prospectus was accurate on the date of the front cover of this prospectus only, and that any information we have incorporated by reference was accurate on the date of the document incorporated by reference only. Our business, financial condition, results of operations and prospects may have changed since such date.

### **INCORPORATION OF CERTAIN INFORMATION BY REFERENCE**

The SEC allows us to “incorporate by reference” information that we file with it into this prospectus, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is an important part of this prospectus. The information incorporated by reference is considered to be a part of this prospectus, and information that we file later with the SEC will automatically update and supersede information contained in documents filed earlier with the SEC or contained in this prospectus and any accompanying prospectus supplement.

We incorporate by reference the documents listed below that we have previously filed with the SEC:

- our Annual Report on Form 10-K for the fiscal year ended December 31, 2016, filed with the SEC on March 16, 2016;
- our Quarterly Report on Form 10-Q for the fiscal quarter ended March 31, 2017, filed with the SEC on May 10, 2017;
- our Quarterly Report on Form 10-Q for the fiscal quarter ended June 30, 2017, filed with the SEC on August 7, 2017;
- our Proxy Statements on Schedule 14A filed with the SEC on April 27, 2017 and July 13, 2017;
- our Current Report on Form 8-K filed with the SEC on June 22, 2017;
- our Current Report on Form 8-K filed with the SEC on June 23, 2017, including the Purchase Agreement and Fifth IRA, copies of which are filed as Exhibits 10.20 and 4.18, respectively, to such Current Report;
- our Current Report on Form 8-K filed with the SEC on June 26, 2017;
- our Current Report on Form 8-K filed with the SEC on August 3, 2017, including the Certificate of Designation and Registration Rights Agreement, copies of which are filed as Exhibits 3.1 and 4.1, respectively, to such Current Report; and
- the description of our common stock contained in our Registration Statement on Form 8-A, filed on October 16, 2014, including any amendments thereto or reports filed for the purposes of updating this description

All reports and other documents that we file with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of the initial registration statement but before the termination of the offering of the Securities hereunder will also be considered to be incorporated by reference into this prospectus from the date of the filing of these reports and documents, and will supersede the information herein; provided, however, that all reports or portions thereof that we “furnish” to the SEC will not be considered incorporated by reference into this prospectus. We undertake to provide without charge to each person (including any beneficial owner) who receives a copy of this prospectus, upon written or oral request, a copy of all of the preceding documents that are incorporated by reference (other than exhibits, unless the exhibits are specifically incorporated by reference into these documents). You may request a copy of these materials in the manner set forth under the heading “Additional Information,” above.

**22,112,775 Shares  
of  
Common Stock**



**PROSPECTUS**

\_\_\_\_\_, 2017

## PART II

### INFORMATION NOT REQUIRED IN THE PROSPECTUS

#### Item 14. Other Expenses of Issuance and Distribution.

Set forth below is an estimate (except in the case of the registration fee) of the amount of fees and expenses to be incurred in connection with the issuance and distribution of the offered securities registered hereby, other than underwriting discounts and commission, if any, incurred in connection with the sale of the offered securities. All such amounts will be borne by Proteon Therapeutics, Inc.

SEC Registration Fee	\$	3,434
Accounting Fees and Expenses	\$	10,000
Legal Fees and Expenses	\$	44,000
Miscellaneous Fees and Expenses	\$	-
Total	\$	57,434

#### Item 15. Indemnification of Directors and Officers.

Under Section 145 of the Delaware Law, the registrant has broad powers to indemnify its directors and officers against liabilities they may incur in such capacities, including liabilities under the Securities Act.

The registrant's certificate of incorporation and bylaws include provisions which (i) eliminate the personal liability of its directors for monetary damages resulting from breaches of their fiduciary duty to the extent permitted by Delaware Law and (ii) require the registrant to indemnify its directors, officers, employees and agents to the fullest extent permitted by Delaware Law, including circumstances in which indemnification is otherwise discretionary. Pursuant to Section 145 of the Delaware Law, a corporation generally has the power to indemnify its present and former directors, officers, employees and agents against expenses incurred by them in connection with any suit to which they are, or are threatened to be made, a party by reason of their serving in such positions so long as they acted in good faith and in a manner they reasonably believed to be in or not opposed to, the best interests of the corporation and, with respect to any criminal action, had no reasonable cause to believe their conduct was unlawful. The registrant believes that these provisions are necessary to attract and retain qualified persons as directors and executive officers. These provisions do not eliminate the directors' duty of care, and, in appropriate circumstances, equitable remedies such as injunctive or other forms of non-monetary relief will remain available under Delaware Law. In addition, each director will continue to be subject to liability for breach of the director's duty of loyalty to the registrant, for acts or omissions not in good faith or involving intentional misconduct, for knowing violations of law, for acts or omissions that the director believes to be contrary to the registrant's best interests or the best interests of the registrant's stockholders, for any transaction from which the director derived an improper personal benefit, and any act related to unlawful stock repurchases, redemptions or other distribution or payments of dividends. The provision also does not affect a director's responsibilities under any other law, such as the federal securities law or state or federal environmental laws.

The registrant has entered into indemnity agreements with certain of its directors and executive officers that require the registrant to indemnify such persons against expenses, judgments, fines, settlements and other amounts incurred (including expenses of a derivative action) in connection with any proceeding, whether actual or threatened, to which any such person may be made a party by reason of the fact that such person is or was one of the registrant's directors or executive officers, provided, among other things, that such person's conduct was not knowingly fraudulent or deliberately dishonest or constituted willful misconduct. The indemnification agreements also set forth certain procedures that will apply in the event of a claim for indemnification thereunder.

At present, there is no pending litigation or proceeding involving any of the registrant's directors or executive officers as to which indemnification is being sought nor is the registrant aware of any threatened litigation that may result in claims for indemnification by any executive officer or director.

We also maintain directors' and officers' liability insurance which covers certain liabilities of our directors and officers arising out of claims based on acts or omissions in their capacities as directors or officers, including liabilities under the Securities Act.

## Item 16. Exhibits.

The exhibits required by Item 601 of Regulation S-K and Item 16 of this Amendment No. 1 to Registration Statement on Form S-3 are listed in the Exhibit Index immediately preceding the exhibits and such list is incorporated herein by reference.

## Item 17. Undertakings.

(a) The undersigned registrant hereby undertakes:

(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

(i) To include any prospectus required by Section 10(a)(3) of the Securities Act.

(ii) To reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20% change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement.

(iii) To include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement.

*provided, however*, that paragraphs (i), (ii) and (iii) do not apply if the registration statement is on Form S-3 and the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the Commission by the registrant pursuant to Section 13 or Section 15(d) of the Exchange Act that are incorporated by reference in the registration statement, or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of the registration statement;

(2) That, for the purpose of determining any liability under the Securities Act, each such post-effective amendment 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.

(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

(5) That, for the purpose of determining liability under the Securities Act to any purchaser:

(i) If the registrant is relying on Rule 430B,

(A) Each prospectus filed by the registrant pursuant to Rule 424(b)(3) shall be deemed to be part of the registration statement as of the date the filed prospectus was deemed part of and included in the registration statement; and

(B) Each prospectus required to be filed pursuant to Rule 424(b)(2), (b)(5) or (b)(7) as part of a registration statement in reliance on Rule 430B relating to an offering made pursuant to Rule 415(a)(1)(i), (vii) or (x) for the purpose of providing the information required by Section 10(a) of the Securities Act of 1933 shall be deemed to be part of and included in the registration statement as of the earlier of the date such form of prospectus is first used after effectiveness or the date of the first contract of sale of securities in the offering described in the prospectus. As provided in Rule 430B, for liability purposes of the issuer and any person that is at that date an underwriter, such date shall be deemed to be a new effective date of the registration statement relating to the securities in the registration statement to which that prospectus relates, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof. Provided, however, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such effective date, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such effective date; or



(ii) If the registrant is subject to Rule 430C, each prospectus filed pursuant to Rule 424(b) as part of a registration statement relating to an offering, other than registration statements relying on Rule 430B or other than prospectuses filed in reliance on Rule 430A, shall be deemed to be part of and included in the registration statement as of the date it is first used after effectiveness; provided, however, that no statement made in a registration statement or prospectus that is part of the registration statement or made in a document incorporated or deemed incorporated by reference into the registration statement or prospectus that is part of the registration statement will, as to a purchaser with a time of contract of sale prior to such first use, supersede or modify any statement that was made in the registration statement or prospectus that was part of the registration statement or made in any such document immediately prior to such date of first use.

(b) The undersigned registrant hereby undertakes that, for purposes of determining any liability under the Securities Act, each filing of the registrant's annual report pursuant to Section 13(a) or Section 15(d) of the Exchange Act that is incorporated by reference in this registration statement 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.

(c) 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.

## SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and 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 this August 14, 2017.

### PROTEON THERAPEUTICS, INC.

By: /s/ Timothy P. Noyes  
Timothy P. Noyes  
President, Chief Executive Officer and Director

Pursuant to the requirements of the Securities Act of 1933, this registration statement has been signed by the following persons in the capacities and on the dates indicated.

<b>Signature</b>	<b>Title</b>	<b>Date</b>
<u>/s/ Timothy P. Noyes</u> Timothy P. Noyes	President, Chief Executive Officer and Director (Principal Executive Officer)	August 14, 2017
<u>/s/ George A. Eldridge</u> George A. Eldridge	Senior Vice President, Chief Financial Officer, Treasurer and Assistant Secretary (Principal Financial and Accounting Officer)	August 14, 2017
<u>/s/ Hubert Birner</u> Hubert Birner	Director	August 14, 2017
<u>/s/ Garen Bohlin</u> Garen Bohlin	Director	August 14, 2017
<u>/s/ Scott A. Canute</u> Scott A. Canute	Director	August 14, 2017
<u>/s/ John G. Freund</u> John G. Freund	Director	August 14, 2017
<u>/s/ Timothy Haines</u> Timothy Haines	Director	August 14, 2017
<u>/s/ Paul J. Hastings</u> Paul J. Hastings	Director	August 14, 2017
<u>/s/ Stuart (Anthony) Kingsley</u> Stuart (Anthony) Kingsley	Director	August 14, 2017
<u>/s/ Jonathan S. Leff</u> Jonathan S. Leff	Director	August 14, 2017

## EXHIBIT INDEX

- 3.1 Certificate of Designation of Preferences, Rights and Limitations of Series A Convertible Preferred Stock, dated August 1, 2017 (incorporated by reference to Exhibit 3.1 of Current Report on Form 8-K, filed on August 3, 2017)
- 4.1 Fifth Amended and Restated Investors' Rights Agreement, dated June 22, 2017, by and among Proteon Therapeutics, Inc. and the stockholders party thereto (incorporated by reference to Exhibit 4.18 of Current Report on Form 8-K, filed on June 23, 2017).
- 4.2 Registration Rights Agreement, dated as of August 2, 2017 (incorporated by reference to Exhibit 4.1 of Current Report on Form 8-K, filed on August 3, 2017).
- 5.1# Opinion of Morgan, Lewis & Bockius LLP.
- 10.1 Securities Purchase Agreement, dated as of June 23, 2017, by and among the Company and the purchasers party thereto (incorporated by reference to Exhibit 10.20 of Current Report on Form 8-K, filed on June 23, 2017).
- 23.1\* Consent of Independent Registered Public Accounting Firm.
- 23.2# Consent of Morgan, Lewis and Bockius LLP (included in Exhibit 5.1).

\* Filed herewith

# Previously filed

**CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM**

We consent to the reference to our firm under the caption "Experts" in this Amendment No. 1 to the Registration Statement (Form S-3/A) and related Prospectus of Proteon Therapeutics, Inc. for the registration of Common Stock and to the incorporation by reference therein of our report dated March 16, 2017, with respect to the consolidated financial statements of Proteon Therapeutics, Inc. included in its Annual Report (Form 10-K) for the year ended December 31, 2016, filed with the Securities and Exchange Commission.

/s/ Ernst & Young LLP

Boston, Massachusetts  
August 14, 2017