

**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549**

**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
(I.R.S. Employer
Identification Number)

**200 West Street
Waltham, MA 02451
(781) 890-0102**

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

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

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

Copies to:

**Julio E. Vega, Esq.
William S. Perkins, Esq.
Morgan, Lewis & Bockius LLP
One Federal Street
Boston, MA 02110
(617) 951-8000**

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

From time to time after the effective date of this Registration Statement
(Approximate date of commencement of proposed sale to the public)

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, 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 Exchange Act.

| | | | |
|-------------------------|-------------------------------------|---------------------------|--------------------------|
| Large accelerated filer | <input type="checkbox"/> | Accelerated filer | <input type="checkbox"/> |
| Non-accelerated filer | <input checked="" type="checkbox"/> | Smaller reporting company | <input type="checkbox"/> |

(Do not check if a smaller reporting company)

CALCULATION OF REGISTRATION FEE

| Title of each class of securities to be registered | Amount to be Registered | Proposed Maximum Offering Price per Unit | Proposed Maximum Aggregate Offering Price | Amount of Registration Fee (1) |
|--|-------------------------|--|---|--------------------------------|
| Common Stock, par value \$0.001 per share | (2) | (3) | (3) | -- |
| Preferred Stock, par value \$0.001 per share | (2) | (3) | (3) | -- |
| Debt Securities | (2) | (3) | (3) | -- |
| Warrants | (2) | (3) | (3) | -- |
| Total | (2) | (3) | \$150,000,000 | \$15,105 |

(1) Calculated pursuant to Rule 457(o) under the Securities Act.

(2) There are being registered hereunder such indeterminate number of shares of common stock and preferred stock, such indeterminate principal amount of debt securities and such indeterminate number of warrants to purchase common stock, preferred stock or debt securities as shall have an aggregate initial offering price not to exceed \$150,000,000. If any debt securities are issued at an original issue discount, then the principal amount of such debt securities shall be in such greater amount as shall result in an aggregate initial offering price not to exceed \$150,000,000, less the aggregate dollar amount of all securities previously issued hereunder. Any securities registered hereunder may be sold separately or as units with other securities registered hereunder. The securities registered also include such indeterminate number of shares of common stock and preferred stock and amount of debt securities as may be issued upon conversion of or exchange for preferred stock or debt securities that provide for conversion or exchange, upon exercise of warrants or pursuant to the antidilution provisions of any such securities. In addition, pursuant to Rule 416 under the Securities Act, the shares being registered hereunder include such indeterminate number of shares of common stock and preferred stock as may be issuable with respect to the shares being registered hereunder as a result of stock splits, stock dividends or similar transactions.

(3) The proposed maximum aggregate offering price per class of security will be determined from time to time by the registrant in connection with the issuance by the registrant of the securities registered hereunder and is not specified as to each class of security pursuant to General Instruction II.D. of Form S-3 under the 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 that specifically states that this registration statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933, as amended, or until the registration statement shall become effective on such date as the Securities and Exchange Commission, acting pursuant to said Section 8(a), may determine.

EXPLANATORY NOTE

This registration statement contains:

- a base prospectus which covers the offering, issuance and sale by us of up to \$150 million in the aggregate of the securities identified above from time to time in one or more offerings; and
- a sales agreement prospectus covering the offering, issuance and sale by us of up to a maximum aggregate offering price of \$40 million of our common stock that may be issued and sold under a sales agreement with Cowen and Company, LLC.

The base prospectus immediately follows this explanatory note. The specific terms of any securities to be offered pursuant to the base prospectus will be specified in a prospectus supplement to the base prospectus. The sales agreement prospectus immediately follows the base prospectus. The \$40 million of common stock that may be offered, issued and sold under the sales agreement prospectus is included in the \$150 million of securities that may be offered, issued and sold by us under the base prospectus.

The information in this prospectus is not complete and may be changed. We may not sell these securities or accept an offer to buy 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 it is not soliciting offers to buy these securities in any state where such offer or sale is not permitted.

\$150,000,000



**Common Stock
Preferred Stock
Debt Securities
Warrants**

From time to time, we may offer, issue and sell up to \$150,000,000 of any combination of the securities described in this prospectus in one or more offerings. We may also offer securities as may be issuable upon conversion, redemption, repurchase, exchange or exercise of any securities registered hereunder, including any applicable antidilution provisions.

This prospectus provides a general description of the securities we may offer. Each time we offer securities, we will provide specific terms of the securities offered in a supplement to this prospectus. We may also authorize one or more free writing prospectuses to be provided to you in connection with these offerings. The prospectus supplement and any related free writing prospectus may also add, update or change information contained in this prospectus. You should carefully read this prospectus, the applicable prospectus supplement and any related free writing prospectus, as well as any documents incorporated by reference, before you invest in any of the securities being offered.

This prospectus may not be used to consummate a sale of any securities unless accompanied by a prospectus supplement.

Our common stock is listed on The NASDAQ Global Market under the symbol "PRTO." On November 11, 2015, the last reported sales price of our common stock was \$14.74 per share. The applicable prospectus supplement will contain information, where applicable, as to any other listing on The NASDAQ Global Market or any securities market or other exchange of the securities, if any, covered by the prospectus supplement.

We will sell these securities directly to investors, through agents designated from time to time or to or through underwriters or dealers, on a continuous or delayed basis. For additional information on the methods of sale, you should refer to the section entitled "Plan of Distribution" in this prospectus. If any agents or underwriters are involved in the sale of any securities with respect to which this prospectus is being delivered, the names of such agents or underwriters and any applicable fees, commissions, discounts or option to purchase additional securities will be set forth in a prospectus supplement. The price to the public of such securities and the net proceeds we expect to receive from such sale will also be set forth in a prospectus supplement.

Investing in our securities involves a high degree of risk. You should review carefully the risks and uncertainties described under the heading "Risk Factors" contained in the applicable prospectus supplement and any related free writing prospectus, and under similar headings in the other documents that are 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 DETERMINED IF THIS PROSPECTUS IS TRUTHFUL OR COMPLETE. ANY REPRESENTATION TO THE CONTRARY IS A CRIMINAL OFFENSE.

The date of this prospectus is _____, 2015

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ABOUT THIS PROSPECTUS

This prospectus is a part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission, or SEC, utilizing a “shelf” registration process. Under this shelf registration process, we may sell any combination of the securities described in this prospectus in one or more offerings up to a total aggregate offering price of \$150 million. This prospectus provides you with a general description of the securities we may offer.

Each time we sell securities under this prospectus, we will provide a prospectus supplement that will contain specific information about the terms of that offering. We may also authorize one or more free writing prospectuses to be provided to you that may contain material information relating to these offerings. The prospectus supplement and any related free writing prospectus that we may authorize to be provided to you may also add, update or change information contained in this prospectus or in any documents that we have incorporated by reference into this prospectus. You should read this prospectus, any applicable prospectus supplement and any related free writing prospectus, together with the information incorporated herein by reference as described under the heading “Incorporation of Certain Information By Reference,” before investing in any of the securities offered.

This prospectus may not be used to consummate a sale of securities unless it is accompanied by a prospectus supplement.

Neither we, nor any agent, underwriter or dealer has authorized any person to give any information or to make any representation other than those contained or incorporated by reference in this prospectus, any applicable prospectus supplement or any related free writing prospectus prepared by or on behalf of us or to which we have referred you. This prospectus, any applicable supplement to this prospectus or any related free writing prospectus do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the registered securities to which they relate, nor does this prospectus, any applicable supplement to this prospectus or any related free writing prospectus constitute an offer to sell or the solicitation of an offer to buy securities in any jurisdiction to any person to whom it is unlawful to make such offer or solicitation in such jurisdiction.

You should not assume that the information contained in this prospectus, any applicable prospectus supplement or any related free writing 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, any applicable prospectus supplement or any related free writing prospectus is delivered, or securities are sold, on a later date.

This prospectus contains summaries of certain provisions contained in some of the documents described herein, but reference is made to the actual documents for complete information. All of the summaries are qualified in their entirety by the actual documents. Copies of some of the documents referred to herein have been filed, will be filed or will be incorporated by reference as exhibits to the registration statement of which this prospectus is a part, and you may obtain copies of those documents as described below under the heading “Where You Can Find More Information.”

SUMMARY

This summary highlights selected information from this prospectus and does not contain all of the information that you need to consider in making your investment decision. You should carefully read the entire prospectus, the applicable prospectus supplement and any related free writing prospectus, including the risks of investing in our securities discussed under the heading “Risk Factors” contained in the applicable prospectus supplement and any related free writing prospectus, and under similar headings in the other documents that are incorporated by reference into this prospectus. You should also carefully read the information incorporated by reference into this prospectus, including our consolidated financial statements, and the exhibits to the registration statement of which this prospectus is a part.

Unless the context indicates otherwise, as used in this prospectus, the terms “Proteon,” “the Company,” “we,” “us” and “our” refer to Proteon Therapeutics, Inc., a Delaware corporation, and, where appropriate, our consolidated subsidiary.

Company Overview

Proteon Therapeutics, Inc. is 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 (formerly PRT-201), is a recombinant human elastase that we are developing to improve arteriovenous fistula, or AVF patency, in patients with chronic kidney disease undergoing or preparing for hemodialysis, a lifesaving treatment that cannot be conducted without a functioning vascular access. We believe the data from our completed Phase 2 trial of vonapanitase in patients undergoing creation of an arteriovenous fistula, or AVF, support that a one-time, local application of vonapanitase during AVF surgical placement reduces AVF failure, thereby improving patient outcomes and reducing the burden on patients and the healthcare system. We are not aware of any approved preventative treatments to reduce the failure rate of AVFs. We enrolled the first patient in the first of two Phase 3 trials for vonapanitase in radiocephalic AVFs, our initial indication, in the third quarter of 2014 and subsequently completed patient enrollment in October 2015. We enrolled the first patient in our second Phase 3 trial in August 2015. Data from our first Phase 3 trial is expected in December 2016.

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.

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. The information contained in, or that can be accessed through, our website is not part of this prospectus.

The Securities We May Offer

We may offer shares of our common stock and preferred stock, various series of debt securities and warrants to purchase any of such securities, up to a total aggregate offering price of \$150,000,000 from time to time in one or more offerings under this prospectus, together with any applicable prospectus supplement and any related free writing prospectus, at prices and on terms to be determined by market conditions at the time of the relevant offering. This prospectus provides you with a general description of the securities we may offer.

Each time we offer a type or series of securities under this prospectus, we will provide a prospectus supplement that will describe the specific amounts, prices and other important terms of the securities, including, to the extent applicable:

- designation or classification;
 - aggregate principal amount or aggregate offering price;
 - maturity, if applicable;
-

- original issue discount, if any;
- rates and times of payment of interest or dividends, if any;
- redemption, conversion, exchange or sinking fund terms, if any;
- conversion or exchange prices or rates, if any, and, if applicable, any provisions for changes to or adjustments in the conversion or exchange prices or rates and in the securities or other property receivable upon conversion or exchange;
- ranking, if applicable;
- restrictive covenants, if any;
- voting or other rights, if any; and
- important United States federal income tax considerations.

The prospectus supplement and any related free writing prospectus that we may authorize to be provided to you may also add, update or change information contained in this prospectus or in documents we have incorporated by reference. However, no prospectus supplement or free writing prospectus will offer a security that is not registered and described in this prospectus at the time of the effectiveness of the registration statement of which this prospectus is a part.

This prospectus may not be used to consummate a sale of securities unless it is accompanied by a prospectus supplement.

We may sell the securities directly to investors or through underwriters, dealers or agents. We, and our underwriters or agents, reserve the right to accept or reject all or part of any proposed purchase of securities. If we do offer securities through underwriters or agents, we will include in the applicable prospectus supplement:

- the names of those underwriters or agents;
- applicable fees, discounts and commissions to be paid to them;
- details regarding option to purchase additional securities, if any; and
- the estimated net proceeds to us.

Common stock. We may issue shares of our common stock from time to time. Each holder of our common stock is entitled to one vote for each share on all matters submitted to a vote of the stockholders, including the election of directors. Our stockholders do not have cumulative voting rights in the election of directors. An election of directors by our stockholders shall be determined by a plurality of votes cast by the stockholders entitled to vote on the election. Subject to preferences that may be applicable to any then outstanding preferred stock, holders of our common stock are entitled to receive dividends, if any, as may be declared from time to time by our board of directors out of legally available funds. In the event of our liquidation, dissolution or winding up, holders of our common stock will be entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of all of our debts and other liabilities and the satisfaction of any liquidation preference granted to the holders of any then outstanding shares of preferred stock. Holders of common stock have no preemptive, conversion or subscription rights and there are no redemption or sinking fund provisions applicable to the common stock. The rights, preferences and privileges of the holders of common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of preferred stock that we may designate in the future. When we issue shares of common stock under this prospectus, the shares will be fully paid and non-assessable. In this prospectus, we have summarized certain general features of our common stock under “Description of Capital Stock-Common Stock.” We urge you, however, to read the applicable prospectus supplement (and any related free writing prospectus that we may authorize to be provided to you) related to any common stock being offered.

Preferred stock. We may issue shares of our preferred stock from time to time, in one or more series. Under our amended and restated certificate of incorporation, our board of directors has the authority, without further action by the stockholders, to issue up to 10,000,000 shares of preferred stock in one or more series, to establish from time to time the number of shares to be included in each such series, to fix the rights, preferences and privileges of the shares of each wholly unissued series and any qualifications, limitations or restrictions thereon and to increase or decrease the number of shares of any such series, but not below the number of shares of such series then outstanding. Since our amended and restated certificate of incorporation became effective, we have not designated or issued any series of preferred stock, and therefore we are not offering previously designated series of preferred stock under this prospectus. If we sell any new series of preferred stock under this prospectus and any applicable prospectus supplement, our board of directors will determine the designations, voting powers, preferences and rights of the preferred stock being offered, as well as the qualifications, limitations or restrictions thereof, including dividend rights, conversion rights, preemptive rights, terms of redemption or repurchase, liquidation preferences, sinking fund terms and the number of shares constituting any series or the designation of any series. Convertible preferred stock may be convertible into our common stock or exchangeable for our other securities. Conversion may be mandatory or at the holder's option and would be at prescribed conversion rates. We will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of the certificate of designation that describes the terms of the series of preferred stock that we are offering before the issuance of the related series of preferred stock. In this prospectus, we have summarized certain general features of the preferred stock under "Description of Capital Stock-Preferred Stock." We urge you, however, to read the applicable prospectus supplement (and any related free writing prospectus that we may authorize to be provided to you) related to the series of preferred stock being offered, as well as the complete certificate of designation that contains the terms of the applicable series of preferred stock.

Debt securities. We may issue debt securities from time to time, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. The senior debt securities will rank equally with any other unsecured and unsubordinated debt. The subordinated debt securities will be subordinate and junior in right of payment, to the extent and in the manner described in the instrument governing the debt, to all of our senior indebtedness. Convertible debt securities will be convertible into our common stock or preferred stock. Conversion may be mandatory or at the holder's option and would be at prescribed conversion rates.

The debt securities will be issued under one or more documents called indentures, which are contracts between us and a national banking association or other eligible party, as trustee. In this prospectus, we have summarized certain general features of the debt securities. We urge you, however, to read the applicable prospectus supplement (and any free writing prospectus that we may authorize to be provided to you) related to the series of debt securities being offered, as well as the complete indentures that contain the terms of the debt securities. A form of indenture has been filed as an exhibit to the registration statement of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of the debt securities being offered will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

Warrants. We may issue warrants for the purchase of common stock, preferred stock and/or debt securities in one or more series. We may issue warrants independently or together with common stock, preferred stock and/or debt securities, and the warrants may be attached to or separate from these securities. In this prospectus, we have summarized certain general features of the warrants. We urge you, however, to read the applicable prospectus supplement (and any free writing prospectus that we may authorize to be provided to you) related to the particular series of warrants being offered, as well as the complete warrant agreements and warrant certificates that contain the terms of the warrants. Forms of the warrant agreements and forms of warrant certificates containing the terms of the warrants to be offered will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

We will evidence each series of warrants by warrant certificates that we will issue. Warrants may be issued under an applicable warrant agreement that we enter into with a warrant agent. We will indicate the name and address of the warrant agent, if applicable, in the prospectus supplement relating to the particular series of warrants being offered.

RISK FACTORS

Investing in our securities involves a high degree of risk. You should carefully review the risks and uncertainties described under the heading “Risk Factors” contained in any applicable prospectus supplement and any related free writing prospectus, and under similar headings in our Annual Report on Form 10-K for the year ended December 31, 2014, as updated by our annual, quarterly and other reports and documents that are incorporated by reference into this prospectus, before deciding whether to purchase any of the securities being registered pursuant to the registration statement of which this prospectus is a part. Each of the risk factors could adversely affect our business, operating results and financial condition, as well as adversely affect the value of an investment in our securities, and the occurrence of any of these risks might cause you to lose all or part of your investment. Additional risks not presently known to us or that we currently believe are immaterial may also significantly impair our business operations. Please also read carefully the section below titled “Special Note Regarding Forward-Looking Statements.”

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, each prospectus supplement and the information incorporated by reference in this prospectus and each prospectus supplement contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, which we refer to as the Securities Act, and Section 21E of the Exchange Act of 1934, as amended, which we refer to as the Exchange Act, that involve a number of risks and uncertainties. Although our forward-looking statements reflect the good faith judgment of our management, these statements can only be based on facts and factors currently known by us. Consequently, these forward-looking statements are inherently subject to risks and uncertainties, and actual results and outcomes may differ materially from results and outcomes discussed in the forward-looking statements.

Forward-looking statements can be identified by the use of forward-looking words such as “believes,” “expects,” “hopes,” “may,” “will,” “plan,” “intends,” “estimates,” “could,” “should,” “would,” “continue,” “seeks,” “pro forma,” or “anticipates,” or other similar words (including their use in the negative), or by discussions of future matters. These statements include but are not limited to statements under the captions “Business,” “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and in other sections included in any applicable prospectus supplement or incorporated by reference from our Annual Report on Form 10-K and Quarterly Reports on Form 10-Q, as applicable, as well as our other filings with the SEC. You should be aware that the occurrence of any of the events discussed under the heading “Risk Factors” in any applicable prospectus supplement and any documents incorporated by reference herein or therein could substantially harm our business, operating results and financial condition and that if any of these events occurs, it could adversely affect the value of an investment in our securities.

The cautionary statements made in this prospectus are intended to be applicable to all related forward-looking statements wherever they may appear in this prospectus or in any prospectus supplement or any documents incorporated by reference herein or therein. We urge you not to place undue reliance on these forward-looking statements, which speak only as of the date they are made. Except as required by law, we assume no obligation to update our forward-looking statements, even if new information becomes available in the future.

RATIO OF EARNINGS TO FIXED CHARGES

Any time debt securities are offered pursuant to this prospectus, we will provide a table setting forth our ratio of earnings to fixed charges on a historical basis in the applicable prospectus supplement, if required.

USE OF PROCEEDS

We will retain broad discretion over the use of the net proceeds from the sale of the securities offered hereby. Except as described in any prospectus supplement or any related free writing prospectus that we may authorize to be provided to you, we currently intend to use the net proceeds from the sale of the securities offered hereby for general corporate purposes, which may include capital expenditures, working capital and general and administrative expenses. We may also use a portion of the net proceeds to acquire or invest in businesses that are complementary to our own, although we have no current plans, commitments or agreements with respect to any acquisitions as of the date of this prospectus. We will set forth in the applicable prospectus supplement or free writing prospectus our intended use for the net proceeds received from the sale of any securities sold pursuant to the prospectus supplement or free writing prospectus. Pending these uses, we intend to invest the net proceeds in short-term obligations of the U.S. government and its agencies.

DESCRIPTION OF CAPITAL STOCK

The description below of our capital stock and provisions of our amended and restated certificate of incorporation and amended and restated bylaws are summaries and are qualified by reference to the amended and restated certificate of incorporation, the amended and restated bylaws, and the applicable provisions of Delaware law.

General

Our amended and restated certificate of incorporation authorizes us to issue up to 100,000,000 shares of common stock, \$0.001 par value per share, and 10,000,000 shares of preferred stock, \$0.001 par value per share.

As of October 31, 2015, there were 16,484,508 shares of common stock outstanding, no shares of preferred stock outstanding, and no warrants for the purchase of shares of capital stock outstanding.

Common Stock

Voting rights. Each holder of our common stock is entitled to one vote for each share on all matters submitted to a vote of the stockholders, including the election of directors. Our stockholders do not have cumulative voting rights in the election of directors. An election of directors by our stockholders shall be determined by a plurality of votes cast by the stockholders entitled to vote on the election.

Dividends. Subject to preferences that may be applicable to any then outstanding preferred stock, holders of our common stock are entitled to receive dividends, if any, as may be declared from time to time by our board of directors out of legally available funds.

Liquidation. In the event of our liquidation, dissolution or winding up, holders of our common stock will be entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of all of our debts and other liabilities and the satisfaction of any liquidation preference granted to the holders of any then outstanding shares of preferred stock.

Rights and preferences. Holders of common stock have no preemptive, conversion or subscription rights and there are no redemption or sinking fund provisions applicable to the common stock. The rights, preferences and privileges of the holders of common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of preferred stock that we may designate in the future.

Fully paid and nonassessable. All of our outstanding shares of common stock are, and the shares of common stock to be issued in this offering, if any, will be, fully paid and nonassessable.

Preferred Stock

Under our amended and restated certificate of incorporation, our board of directors has the authority, without further action by the stockholders (unless such stockholder action is required by applicable law or the rules of any stock exchange or market on which our securities are then traded), to designate and issue up to 10,000,000 shares of preferred stock in one or more series, to establish from time to time the number of shares to be included in each such series, to fix the rights, preferences and privileges of the shares of each wholly unissued series and any qualifications, limitations or restrictions thereon and to increase or decrease the number of shares of any such series, but not below the number of shares of such series then outstanding.

We will fix the designations, voting powers, preferences and rights of the preferred stock of each series, as well as the qualifications, limitations or restrictions thereof, in a certificate of designation relating to that series. We will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of any certificate of designation that describes the terms of the series of preferred stock we are offering before the issuance of that series of preferred stock. This description will include:

- the title and stated value;
- the number of shares we are offering;

- the liquidation preference per share;
- the purchase price;
- the dividend rate, period and payment date and method of calculation for dividends;
- whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;
- the procedures for any auction and remarketing, if any;
- the provisions for a sinking fund, if any;
- the provisions for redemption or repurchase, if applicable, and any restrictions on our ability to exercise those redemption and repurchase rights;
- any listing of the preferred stock on any securities exchange or market;
- whether the preferred stock will be convertible into our common stock, and, if applicable, the conversion price, or how it will be calculated, and the conversion period;
- whether the preferred stock will be exchangeable into debt securities, and, if applicable, the exchange price, or how it will be calculated, and the exchange period;
- voting rights, if any, of the preferred stock;
- preemptive rights, if any;
- restrictions on transfer, sale or other assignment, if any;
- whether interests in the preferred stock will be represented by depositary shares;
- a discussion of any material U.S. federal income tax considerations applicable to the preferred stock;
- the relative ranking and preferences of the preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs;
- any limitations on the issuance of any class or series of preferred stock ranking senior to or on a parity with the series of preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs; and
- any other specific terms, preferences, rights or limitations of, or restrictions on, the preferred stock.

Delaware law provides that the holders of preferred stock will have the right to vote separately as a class (or, in some cases, as a series) on an amendment to our certificate of incorporation if the amendment would change the par value or, unless the certificate of incorporation provided otherwise, the number of authorized shares of the class or change the powers, preferences or special rights of the class or series so as to adversely affect the class or series, as the case may be. This right is in addition to any voting rights that may be provided for in the applicable certificate of designation.

Our board of directors may authorize the issuance of preferred stock with voting or conversion rights that could adversely affect the voting power or other rights of the holders of the common stock. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions and other corporate purposes, could, among other things, have the effect of delaying, deferring or preventing a change in our control that may otherwise benefit holders of our common stock and may adversely affect the market price of the common stock and the voting and other rights of the holders of common stock.

Warrants

As of October 31, 2015, we had no outstanding warrants to purchase shares of our capital stock.

Registration Rights

We agreed to provide certain registration rights to certain holders of our common stock pursuant to the terms of the Fourth Amended and Restated Investor's Rights Agreement, or IRA. We entered into the IRA in connection with the issuance of our Series D convertible preferred stock (which converted to common stock in our IPO) on May 13, 2014, and further amended the IRA on October 8, 2013 and February 5, 2014.

Anti-Takeover Effects of Provisions of Our Amended and Restated Certificate of Incorporation and Bylaws

Our amended and restated certificate of incorporation and amended and restated bylaws contain certain provisions that are intended to enhance the likelihood of continuity and stability in the composition of the board of directors and which may have the effect of delaying, deferring or preventing a future takeover or change in control of the Company unless such takeover or change in control is approved by the board of directors. These provisions include:

Classified Board. Our amended and restated certificate of incorporation provides that our board of directors will be divided into three classes of directors, with the classes as nearly equal in number as possible. At each annual meeting of the stockholders, a class of directors will be elected for a three-year term to succeed the directors of the same class whose terms are then expiring. As a result approximately one-third of our directors will be elected each year. The current term of office of the directors of Class I shall expire as of the annual meeting of the Company's stockholders taking place in fiscal year 2018; the initial term of office of the directors of Class II shall expire as of the annual meeting of the Company's stockholders taking place in fiscal year 2016; and the initial term of office of the directors of Class III shall expire as of the annual meeting of the Company's stockholders taking place in fiscal year 2017. The classification of directors will have the effect of making it more difficult for stockholders to change the composition of our board.

- Our Class I directors are Timothy Noyes, Garen Bohlin and John Freund;
- Our Class II directors are Hubert Birner, Dmitry Kobzyev, Gregory Phelps and Stuart Kingsley; and
- Our Class III directors are Brendan O'Leary, Tim Haines and Scott Canute.

Our amended and restated certificate of incorporation also provides that, subject to any rights of holders of preferred stock to elect additional directors under specified circumstances, the number of directors will be fixed exclusively pursuant to a resolution adopted by our board of directors. Any additional directorships resulting from an increase in the number of directors will be distributed among the three classes so that, as nearly as possible, each class shall consist of one third of the board of directors. Our board of directors currently has eight members.

Action by Written Consent; Special Meetings of Stockholders. Our amended and restated certificate of incorporation provides that stockholder action can be taken only at an annual or special meeting of stockholders and cannot be taken by written consent in lieu of a meeting. Our amended and restated certificate of incorporation and our amended and restated bylaws also provide that, except as otherwise required by law, special meetings of the stockholders can be called only by or at the direction of the board of directors pursuant to a resolution adopted by a majority of the total number of directors. Except as described above, stockholders are not permitted to call a special meeting or to require the board of directors to call a special meeting.

Removal of Directors. Our amended and restated certificate of incorporation provides that our directors may be removed only for cause by the affirmative vote of at least 75% of the voting power of our outstanding shares of capital stock, voting together as a single class and entitled to vote in the election of directors. This requirement of a supermajority vote to remove directors could enable a minority of our stockholders to prevent a change in the composition of our board.

Advance Notice Procedures. Our amended and restated bylaws establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to the board of directors. Stockholders at an annual meeting are only able to consider proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of the board of directors or by a stockholder who was a stockholder of record on the record date for the meeting, who is entitled to vote at the meeting and who has given our Secretary timely written notice, in proper form, of the stockholder's intention to bring that business before the meeting. Although the amended and restated bylaws do not give the board of directors the power to approve or disapprove stockholder nominations of candidates or proposals regarding other business to be conducted at a special or annual meeting, the amended and restated bylaws may have the effect of precluding the conduct of certain business at a meeting if the proper procedures are not followed or may discourage or deter a potential acquirer from conducting a solicitation of proxies to elect its own slate of directors or otherwise attempting to obtain control of the company.

Super Majority Approval Requirements. The Delaware General Corporation Law generally provides that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation's certificate of incorporation or bylaws, unless either a corporation's certificate of incorporation or bylaws requires a greater percentage. Our amended and restated certificate of incorporation and amended and restated bylaws provide that the affirmative vote of holders of at least 75% of the outstanding shares of capital stock, voting together as a single class and entitled to vote in the election of directors will be required to amend, alter, change or repeal the amended and restated bylaws and the amended and restated certificate of incorporation. This requirement of a supermajority vote to approve amendments to our amended and restated certificate of incorporation and amended and restated bylaws could enable a minority of our stockholders to exercise veto power over any such amendments.

Authorized but Unissued Shares. Our authorized but unissued shares of common stock and preferred stock will be available for future issuance without stockholder approval. These additional shares may be utilized for a variety of corporate purposes, including future public offerings to raise additional capital, corporate acquisitions and employee benefit plans. The existence of authorized but unissued shares of common stock and preferred stock could render more difficult or discourage an attempt to obtain control of a majority of our common stock by means of a proxy contest, tender offer, merger or otherwise.

Exclusive Forum. Our amended and restated certificate of incorporation provides that, subject to limited exceptions, the state or federal courts located in the State of Delaware will be the sole and exclusive forum for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or other employees to us or our stockholders, (iii) any action asserting a claim against us arising pursuant to any provision of the Delaware General Corporation Law, our amended and restated certificate of incorporation or our amended and restated bylaws, or (iv) any other action asserting a claim against us that is governed by the internal affairs doctrine. Any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock shall be deemed to have notice of and to have consented to the provisions of our amended and restated certificate of incorporation described above. Although we believe these provisions benefit us by providing increased consistency in the application of Delaware law for the specified types of actions and proceedings, the provisions may have the effect of discouraging lawsuits against our directors and officers. The enforceability of similar choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that, in connection with one or more actions or proceedings described above, a court could find the choice of forum provisions contained in our amended and restated certificate of incorporation to be inapplicable or unenforceable.

Section 203 Of Delaware Law

We are subject to Section 203 of Delaware Law, or Section 203. In general, Section 203 prohibits a publicly-held Delaware corporation from engaging in a "business combination" with an "interested stockholder" for a three-year period following the time that this stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. A "business combination" includes, among other things, a merger, asset or stock sale or other transaction resulting in a financial benefit to the interested stockholder. An "interested stockholder" is a person who, together with affiliates and associates, owns, or did own within three years prior to the determination of interested stockholder status, 15% or more of the corporation's voting stock. Under Section 203, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions: before the stockholder became interested, the board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder; upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, shares owned by persons who are directors and also officers, and employee stock plans, in some instances; or at or after the time the stockholder became interested, the business combination was approved by the board of directors of the corporation and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder. A Delaware corporation may "opt out" of these provisions with an express provision in its original certificate of incorporation or an express provision in its certificate of incorporation or bylaws resulting from a stockholders' amendment approved by at least a majority of the outstanding voting shares. We have not opted out of these provisions. As a result, mergers or other takeover or change in control attempts of us may be discouraged or prevented.

Transfer Agent And Registrar

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A. Its address is 250 Royall Street, Canton, Massachusetts 02021. The transfer agent for any series of preferred stock, debt securities or warrants that we may offer under this prospectus will be named and described in the prospectus supplement for that series.

NASDAQ Global Market Listing

Our common stock is listed on The NASDAQ Global Market under the symbol "PRTO."

DESCRIPTION OF DEBT SECURITIES

We may issue debt securities from time to time, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. While the terms we have summarized below will apply generally to any debt securities that we may offer under this prospectus, we will describe the particular terms of any debt securities that we may offer in more detail in the applicable prospectus supplement. The terms of any debt securities offered under a prospectus supplement may differ from the terms described below. Unless the context requires otherwise, whenever we refer to the indenture, we also are referring to any supplemental indentures that specify the terms of a particular series of debt securities.

We will issue the debt securities under the indenture that we will enter into with the trustee named in the indenture. The indenture will be qualified under the Trust Indenture Act of 1939, as amended, or the Trust Indenture Act. We will file the form of indenture as an exhibit to the registration statement of which this prospectus is a part, and supplemental indentures and forms of debt securities containing the terms of the debt securities being offered will be filed as exhibits to the registration statement of which this prospectus is a part or will be incorporated by reference from reports that we file with the SEC.

The following summary of material provisions of the debt securities and the indenture is subject to, and qualified in its entirety by reference to, all of the provisions of the indenture applicable to a particular series of debt securities. We urge you to read the applicable prospectus supplements and any related free writing prospectuses related to the debt securities that we may offer under this prospectus, as well as the complete indenture that contains the terms of the debt securities.

General

The indenture will not limit the amount of debt securities that we may issue. It provides that we may issue debt securities up to the principal amount that we may authorize and may be in any currency or currency unit that we may designate. Except for the limitations on consolidation, merger and sale of all or substantially all of our assets contained in the indenture, the terms of the indenture do not contain any covenants or other provisions designed to give holders of any debt securities protection against changes in our operations, financial condition or transactions involving us.

We may issue the debt securities issued under the indenture as "discount securities," which means they may be sold at a discount below their stated principal amount. These debt securities, as well as other debt securities that are not issued at a discount, may be issued with "original issue discount," or OID, for U.S. federal income tax purposes because of interest payment and other characteristics or terms of the debt securities. Material U.S. federal income tax considerations applicable to debt securities issued with OID will be described in more detail in any applicable prospectus supplement.

We will describe in the applicable prospectus supplement the terms of the series of debt securities being offered, including:

- the title of the series of debt securities;
- any limit upon the aggregate principal amount that may be issued;
- the maturity date or dates;
- the form of the debt securities of the series;
- the applicability of any guarantees;
- whether or not the debt securities will be secured or unsecured, and the terms of any secured debt;
- whether the debt securities rank as senior debt, senior subordinated debt, subordinated debt or any combination thereof, and the terms of any subordination;

- if the price (expressed as a percentage of the aggregate principal amount thereof) at which such debt securities will be issued is a price other than the principal amount thereof, the portion of the principal amount thereof payable upon declaration of acceleration of the maturity thereof, or if applicable, the portion of the principal amount of such debt securities that is convertible into another security or the method by which any such portion shall be determined;
- the interest rate or rates, which may be fixed or variable, or the method for determining the rate and the date interest will begin to accrue, the dates interest will be payable and the regular record dates for interest payment dates or the method for determining such dates;
- our right, if any, to defer payment of interest and the maximum length of any such deferral period;
- if applicable, the date or dates after which, or the period or periods during which, and the price or prices at which, we may, at our option, redeem the series of debt securities pursuant to any optional or provisional redemption provisions and the terms of those redemption provisions;
- the date or dates, if any, on which, and the price or prices at which we are obligated, pursuant to any mandatory sinking fund or analogous fund provisions or otherwise, to redeem, or at the holder's option to purchase, the series of debt securities and the currency or currency unit in which the debt securities are payable;
- the denominations in which we will issue the series of debt securities, if other than denominations of \$1,000 and any integral multiple thereof;
- any and all terms, if applicable, relating to any auction or remarketing of the debt securities of that series and any security for our obligations with respect to such debt securities and any other terms which may be advisable in connection with the marketing of debt securities of that series;
- whether the debt securities of the series shall be issued in whole or in part in the form of a global security or securities; the terms and conditions, if any, upon which such global security or securities may be exchanged in whole or in part for other individual securities; and the depository for such global security or securities;
- if applicable, the provisions relating to conversion or exchange of any debt securities of the series and the terms and conditions upon which such debt securities will be so convertible or exchangeable, including the conversion or exchange price, as applicable, or how it will be calculated and may be adjusted, any mandatory or optional (at our option or the holders' option) conversion or exchange features, the applicable conversion or exchange period and the manner of settlement for any conversion or exchange;
- additions to or changes in the covenants applicable to the particular debt securities being issued, including, among others, the consolidation, merger or sale covenant;
- additions to or changes in the events of default with respect to the securities and any change in the right of the trustee or the holders to declare the principal, premium, if any, and interest, if any, with respect to such securities to be due and payable;
- additions to or changes in or deletions of the provisions relating to covenant defeasance and legal defeasance;
- additions to or changes in the provisions relating to satisfaction and discharge of the indenture;
- additions to or changes in the provisions relating to the modification of the indenture both with and without the consent of holders of debt securities issued under the indenture;
- the currency of payment of debt securities if other than U.S. dollars and the manner of determining the equivalent amount in U.S. dollars;
- whether interest will be payable in cash or additional debt securities at our or the holders' option and the terms and conditions upon which the election may be made;

- the terms and conditions, if any, upon which we will pay amounts in addition to the stated interest, premium, if any, and principal amounts of the debt securities of the series to any holder that is not a “United States person” for federal tax purposes;
- any restrictions on transfer, sale or assignment of the debt securities of the series; and
- any other specific terms, preferences, rights or limitations of, or restrictions on, the debt securities, any other additions or changes in the provisions of the indenture, and any terms that may be required by us or advisable under applicable laws or regulations.

Conversion Or Exchange Rights

We will set forth in the applicable prospectus supplement the terms on which a series of debt securities may be convertible into or exchangeable for our common stock or our other securities. We will include provisions as to settlement upon conversion or exchange and whether conversion or exchange is mandatory, at the option of the holder or at our option. We may include provisions pursuant to which the number of shares of our common stock or our other securities that the holders of the series of debt securities receive would be subject to adjustment.

Consolidation, Merger Or Sale

Unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, the indenture will not contain any covenant that restricts our ability to merge or consolidate, or sell, convey, transfer or otherwise dispose of our assets as an entirety or substantially as an entirety. However, any successor to or acquirer of such assets (other than a subsidiary of ours) must assume all of our obligations under the indenture or the debt securities, as appropriate.

Events Of Default Under The Indenture

Unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, the following are events of default under the indenture with respect to any series of debt securities that we may issue:

- if we fail to pay any installment of interest on any series of debt securities, as and when the same shall become due and payable, and such default continues for a period of 90 days; provided, however, that a valid extension of an interest payment period by us in accordance with the terms of any indenture supplemental thereto shall not constitute a default in the payment of interest for this purpose;
- if we fail to pay the principal of, or premium, if any, on any series of debt securities as and when the same shall become due and payable whether at maturity, upon redemption, by declaration or otherwise, or in any payment required by any sinking or analogous fund established with respect to such series; provided, however, that a valid extension of the maturity of such debt securities in accordance with the terms of any indenture supplemental thereto shall not constitute a default in the payment of principal or premium, if any;
- if we fail to observe or perform any other covenant or agreement contained in the debt securities or the indenture, other than a covenant specifically relating to another series of debt securities, and our failure continues for 90 days after we receive written notice of such failure, requiring the same to be remedied and stating that such is a notice of default thereunder, from the trustee or holders of at least 25% in aggregate principal amount of the outstanding debt securities of the applicable series; and
- if specified events of bankruptcy, insolvency or reorganization occur.

If an event of default with respect to debt securities of any series occurs and is continuing, other than an event of default specified in the last bullet point above, the trustee or the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series, by notice to us in writing, and to the trustee if notice is given by such holders, may declare the unpaid principal of, premium, if any, and accrued interest, if any, of such series of debt securities due and payable immediately. If an event of default specified in the last bullet point above occurs with respect to us, the principal amount of and accrued interest, if any, of each issue of debt securities then outstanding shall be due and payable without any notice or other action on the part of the trustee or any holder.

The holders of a majority in principal amount of the outstanding debt securities of an affected series may waive any default or event of default with respect to the series and its consequences, except defaults or events of default regarding payment of principal, premium, if any, or interest, unless we have cured the default or event of default in accordance with the indenture. Any waiver shall cure the default or event of default.

Subject to the terms of the indenture, if an event of default under an indenture shall occur and be continuing, the trustee will be under no obligation to exercise any of its rights or powers under such indenture at the request or direction of any of the holders of the applicable series of debt securities, unless such holders have offered the trustee reasonable indemnity. The holders of a majority in principal amount of the outstanding debt securities of any series will have the right to direct the time, method and place of conducting any proceeding for any remedy available to the trustee, or exercising any trust or power conferred on the trustee, with respect to the debt securities of that series, provided that:

- the direction so given by the holder is not in conflict with any law or the applicable indenture; and
- subject to its duties under the Trust Indenture Act, the trustee need not take any action that might involve it in personal liability or might be unduly prejudicial to the holders not involved in the proceeding.

A holder of the debt securities of any series will have the right to institute a proceeding under the indenture or to appoint a receiver or trustee, or to seek other remedies only if:

- the holder has given written notice to the trustee of a continuing event of default with respect to that series;
- the holders of at least 25% in aggregate principal amount of the outstanding debt securities of that series have made written request;
- such holders have offered to the trustee indemnity satisfactory to it against the costs, expenses and liabilities to be incurred by the trustee in compliance with the request; and
- the trustee does not institute the proceeding, and does not receive from the holders of a majority in aggregate principal amount of the outstanding debt securities of that series other conflicting directions within 90 days after the notice, request and offer.

These limitations do not apply to a suit instituted by a holder of debt securities if we default in the payment of the principal, premium, if any, or interest on, the debt securities.

We will periodically file statements with the trustee regarding our compliance with specified covenants in the indenture.

Modification Of Indenture; Waiver

Unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, we and the trustee may change an indenture without the consent of any holders with respect to specific matters:

- to cure any ambiguity, defect or inconsistency in the indenture or in the debt securities of any series;
- to comply with the provisions described above under “Description of Debt Securities—Consolidation, Merger or Sale;”
- to provide for uncertificated debt securities in addition to or in place of certificated debt securities;
- to add to our covenants, restrictions, conditions or provisions such new covenants, restrictions, conditions or provisions for the benefit of the holders of all or any series of debt securities, to make the occurrence, or the occurrence and the continuance, of a default in any such additional covenants, restrictions, conditions or provisions an event of default or to surrender any right or power conferred upon us in the indenture;
- to add to, delete from or revise the conditions, limitations, and restrictions on the authorized amount, terms, or purposes of issue, authentication and delivery of debt securities, as set forth in the indenture;

- to make any change that does not adversely affect the interests of any holder of debt securities of any series in any material respect;
- to provide for the issuance of and establish the form and terms and conditions of the debt securities of any series as provided above under “Description of Debt Securities—General” to establish the form of any certifications required to be furnished pursuant to the terms of the indenture or any series of debt securities, or to add to the rights of the holders of any series of debt securities;
- to evidence and provide for the acceptance of appointment under any indenture by a successor trustee; or
- to comply with any requirements of the SEC in connection with the qualification of any indenture under the Trust Indenture Act.

In addition, under the indenture, the rights of holders of a series of debt securities may be changed by us and the trustee with the written consent of the holders of at least a majority in aggregate principal amount of the outstanding debt securities of each series that is affected. However, unless we provide otherwise in the prospectus supplement applicable to a particular series of debt securities, we and the trustee may make the following changes only with the consent of each holder of any outstanding debt securities affected:

- extending the fixed maturity of any debt securities of any series;
- reducing the principal amount, reducing the rate of or extending the time of payment of interest, or reducing any premium payable upon the redemption of any series of any debt securities; or
- reducing the percentage of debt securities, the holders of which are required to consent to any amendment, supplement, modification or waiver.

Discharge

The indenture will provide that we can elect to be discharged from our obligations with respect to one or more series of debt securities, except for specified obligations, including obligations to:

- provide for payment;
- register the transfer or exchange of debt securities of the series;
- replace stolen, lost or mutilated debt securities of the series;
- pay principal of and premium and interest on any debt securities of the series;
- maintain paying agencies;
- hold monies for payment in trust;
- recover excess money held by the trustee;
- compensate and indemnify the trustee; and
- appoint any successor trustee.

In order to exercise our rights to be discharged, we must deposit with the trustee money or government obligations sufficient to pay all the principal of, any premium, if any, and interest on, the debt securities of the series on the dates payments are due.

Form, Exchange And Transfer

We will issue the debt securities of each series only in fully registered form without coupons and, unless we provide otherwise in the applicable prospectus supplement, in denominations of \$1,000 and any integral multiple thereof. The indenture will provide that we may issue debt securities of a series in temporary or permanent global form and as book-entry securities that will be deposited with, or on behalf of, The Depository Trust Company, or DTC, or another depository named by us and identified in the applicable prospectus supplement with respect to that series. To the extent the debt securities of a series are issued in global form and as book-entry, a description of terms relating to any book-entry securities will be set forth in the applicable prospectus supplement.

At the option of the holder, subject to the terms of the indenture and the limitations applicable to global securities described in the applicable prospectus supplement, the holder of the debt securities of any series can exchange the debt securities for other debt securities of the same series, in any authorized denomination and of like tenor and aggregate principal amount.

Subject to the terms of the indenture and the limitations applicable to global securities set forth in the applicable prospectus supplement, holders of the debt securities may present the debt securities for exchange or for registration of transfer, duly endorsed or with the form of transfer endorsed thereon duly executed if so required by us or the security registrar, at the office of the security registrar or at the office of any transfer agent designated by us for this purpose. Unless otherwise provided in the debt securities that the holder presents for transfer or exchange, we will impose no service charge for any registration of transfer or exchange, but we may require payment of any taxes or other governmental charges.

We will name in the applicable prospectus supplement the security registrar, and any transfer agent in addition to the security registrar, that we initially designate for any debt securities. We may at any time designate additional transfer agents or rescind the designation of any transfer agent or approve a change in the office through which any transfer agent acts, except that we will be required to maintain a transfer agent in each place of payment for the debt securities of each series.

If we elect to redeem the debt securities of any series, we will not be required to:

- issue, register the transfer of, or exchange any debt securities of that series during a period beginning at the opening of business 15 days before the day of mailing of a notice of redemption of any debt securities that may be selected for redemption and ending at the close of business on the day of the mailing; or
- register the transfer of or exchange any debt securities so selected for redemption, in whole or in part, except the unredeemed portion of any debt securities we are redeeming in part.

Information Concerning The Trustee

The trustee, other than during the occurrence and continuance of an event of default under an indenture, undertakes to perform only those duties as are specifically set forth in the applicable indenture. Upon an event of default under an indenture, the trustee must use the same degree of care as a prudent person would exercise or use in the conduct of his or her own affairs. Subject to this provision, the trustee is under no obligation to exercise any of the powers given it by the indenture at the request of any holder of debt securities unless it is offered reasonable security and indemnity against the costs, expenses and liabilities that it might incur.

Payment And Paying Agents

Unless we otherwise indicate in the applicable prospectus supplement, we will make payment of the interest on any debt securities on any interest payment date to the person in whose name the debt securities, or one or more predecessor securities, are registered at the close of business on the regular record date for the interest.

We will pay principal of and any premium and interest on the debt securities of a particular series at the office of the paying agents designated by us, except that unless we otherwise indicate in the applicable prospectus supplement, we will make interest payments by check that we will mail to the holder or by wire transfer to certain holders. Unless we otherwise indicate in the applicable prospectus supplement, we will designate the corporate trust office of the trustee as our sole paying agent for payments with respect to debt securities of each series. We will name in the applicable prospectus supplement any other paying agents that we initially designate for the debt securities of a particular series. We will maintain a paying agent in each place of payment for the debt securities of a particular series.

All money we pay to a paying agent or the trustee for the payment of the principal of or any premium or interest on any debt securities that remains unclaimed at the end of two years after such principal, premium or interest has become due and payable will be repaid to us, and the holder of the debt security thereafter may look only to us for payment thereof.

Governing Law

The indenture and the debt securities, and any claim, controversy or dispute arising under or related to the indenture or the debt securities, will be governed by and construed in accordance with the laws of the State of New York, except to the extent that the Trust Indenture Act of 1939 is applicable.

DESCRIPTION OF WARRANTS

The following description, together with the additional information we may include in any applicable prospectus supplements and free writing prospectuses, summarizes the material terms and provisions of the warrants that we may offer under this prospectus, which may consist of warrants to purchase common stock, preferred stock or debt securities and may be issued in one or more series. Warrants may be issued independently or together with common stock, preferred stock or debt securities offered by any prospectus supplement, and may be attached to or separate from those securities. While the terms we have summarized below will apply generally to any warrants that we may offer under this prospectus, we will describe the particular terms of any series of warrants that we may offer in more detail in the applicable prospectus supplement and any applicable free writing prospectus. The terms of any warrants offered under a prospectus supplement may differ from the terms described below. However, no prospectus supplement will fundamentally change the terms that are set forth in this prospectus or offer a security that is not registered and described in this prospectus at the time of its effectiveness.

We will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of warrant agreement, if any, including a form of warrant certificate, that describes the terms of the particular series of warrants we are offering. The following summaries of material provisions of the warrants and the warrant agreements are subject to, and qualified in their entirety by reference to, all the provisions of the warrant agreement and warrant certificate applicable to the particular series of warrants that we may offer under this prospectus. We urge you to read the applicable prospectus supplements related to the particular series of warrants that we may offer under this prospectus, as well as any related free writing prospectuses, and the complete warrant agreements and warrant certificates that contain the terms of the warrants.

General

We will describe in the applicable prospectus supplement the terms relating to a series of warrants being offered, including:

- the title of such securities;
- the offering price or prices and aggregate number of warrants offered;
- the currency or currencies for which the warrants may be purchased;
- if applicable, the designation and terms of the securities with which the warrants are issued and the number of warrants issued with each such security or each principal amount of such security;
- if applicable, the date on and after which the warrants and the related securities will be separately transferable;
- if applicable, the minimum or maximum amount of such warrants which may be exercised at any one time;
- in the case of warrants to purchase debt securities, the principal amount of debt securities purchasable upon exercise of one warrant and the price at which, and currency in which, this principal amount of debt securities may be purchased upon such exercise;
- in the case of warrants to purchase common stock or preferred stock, the number of shares of common stock or preferred stock, as the case may be, purchasable upon the exercise of one warrant and the price at which, and the currency in which, these shares may be purchased upon such exercise;
- the effect of any merger, consolidation, sale or other disposition of our business on the warrant agreements and the warrants;
- the terms of any rights to redeem or call the warrants;

- the terms of any rights to force the exercise of the warrants;
- any provisions for changes to or adjustments in the exercise price or number of securities issuable upon exercise of the warrants;
- the dates on which the right to exercise the warrants will commence and expire;
- the manner in which the warrant agreements and warrants may be modified;
- a discussion of any material or special United States federal income tax consequences of holding or exercising the warrants;
- the terms of the securities issuable upon exercise of the warrants; and
- any other specific terms, preferences, rights or limitations of or restrictions on the warrants.

Before exercising their warrants, holders of warrants will not have any of the rights of holders of the securities purchasable upon such exercise, including:

- in the case of warrants to purchase debt securities, the right to receive payments of principal of, or premium, if any, or interest on, the debt securities purchasable upon exercise or to enforce covenants in the applicable indenture; or
- in the case of warrants to purchase common stock or preferred stock, the right to receive dividends, if any, or, payments upon our liquidation, dissolution or winding up or to exercise voting rights, if any.

Exercise Of Warrants

Each warrant will entitle the holder to purchase the securities that we specify in the applicable prospectus supplement at the exercise price that we describe in the applicable prospectus supplement. Unless we otherwise specify in the applicable prospectus supplement, holders of the warrants may exercise the warrants at any time up to the specified time on the expiration date that we set forth in the applicable prospectus supplement. After the close of business on the expiration date, unexercised warrants will become void.

Unless we otherwise specify in the applicable prospectus supplement, holders of the warrants may exercise the warrants by delivering the warrant certificate representing the warrants to be exercised together with specified information, and paying the required amount to the warrant agent in immediately available funds, as provided in the applicable prospectus supplement. We will set forth on the reverse side of the warrant certificate and in the applicable prospectus supplement the information that the holder of the warrant will be required to deliver to the warrant agent in connection with the exercise of the warrant.

Upon receipt of the required payment and the warrant certificate properly completed and duly executed at the corporate trust office of the warrant agent or any other office indicated in the applicable prospectus supplement, we will issue and deliver the securities purchasable upon such exercise. If fewer than all of the warrants represented by the warrant certificate are exercised, then we will issue a new warrant certificate for the remaining amount of warrants. If we so indicate in the applicable prospectus supplement, holders of the warrants may surrender securities as all or part of the exercise price for warrants.

Governing Law

Unless we provide otherwise in the applicable prospectus supplement, the warrants and warrant agreements, and any claim, controversy or dispute arising under or related to the warrants or warrant agreements, will be governed by and construed in accordance with the laws of the State of New York.

Enforceability Of Rights By Holders Of Warrants

Each warrant agent will act solely as our agent under the applicable warrant agreement and will not assume any obligation or relationship of agency or trust with any holder of any warrant. A single bank or trust company may act as warrant agent for more than one issue of warrants. A warrant agent will have no duty or responsibility in case of any default by us under the applicable warrant agreement or warrant, including any duty or responsibility to initiate any proceedings at law or otherwise, or to make any demand upon us. Any holder of a warrant may, without the consent of the related warrant agent or the holder of any other warrant, enforce by appropriate legal action its right to exercise, and receive the securities purchasable upon exercise of, its warrants.

LEGAL OWNERSHIP OF SECURITIES

We can issue securities in registered form or in the form of one or more global securities. We describe global securities in greater detail below. We refer to those persons who have securities registered in their own names on the books that we or any applicable trustee or depository maintain for this purpose as the “holders” of those securities. These persons are the legal holders of the securities. We refer to those persons who, indirectly through others, own beneficial interests in securities that are not registered in their own names, as “indirect holders” of those securities. As we discuss below, indirect holders are not legal holders, and investors in securities issued in book-entry form or in street name will be indirect holders.

Book-Entry Holders

We may issue securities in book-entry form only, as we will specify in the applicable prospectus supplement. This means securities may be represented by one or more global securities registered in the name of a financial institution that holds them as depository on behalf of other financial institutions that participate in the depository’s book-entry system. These participating institutions, which are referred to as participants, in turn, hold beneficial interests in the securities on behalf of themselves or their customers.

Only the person in whose name a security is registered is recognized as the holder of that security. Global securities will be registered in the name of the depository or its participants. Consequently, for global securities, we will recognize only the depository as the holder of the securities, and we will make all payments on the securities to the depository. The depository passes along the payments it receives to its participants, which in turn pass the payments along to their customers who are the beneficial owners. The depository and its participants do so under agreements they have made with one another or with their customers; they are not obligated to do so under the terms of the securities.

As a result, investors in a global security will not own securities directly. Instead, they will own beneficial interests in a global security, through a bank, broker or other financial institution that participates in the depository’s book-entry system or holds an interest through a participant. As long as the securities are issued in global form, investors will be indirect holders, and not legal holders, of the securities.

Street Name Holders

A global security may be terminated in certain situations as described under “—Special Situations When A Global Security Will Be Terminated,” or issue securities that are not issued in global form. In these cases, investors may choose to hold their securities in their own names or in “street name.” Securities held by an investor in street name would be registered in the name of a bank, broker or other financial institution that the investor chooses, and the investor would hold only a beneficial interest in those securities through an account he or she maintains at that institution.

For securities held in street name, we or any applicable trustee or depository will recognize only the intermediary banks, brokers and other financial institutions in whose names the securities are registered as the holders of those securities, and we or any such trustee or depository will make all payments on those securities to them. These institutions pass along the payments they receive to their customers who are the beneficial owners, but only because they agree to do so in their customer agreements or because they are legally required to do so. Investors who hold securities in street name will be indirect holders, not holders, of those securities.

Legal Holders

Our obligations, as well as the obligations of any applicable trustee or third party employed by us or a trustee, run only to the legal holders of the securities. We do not have obligations to investors who hold beneficial interests in global securities, in street name or by any other indirect means. This will be the case whether an investor chooses to be an indirect holder of a security or has no choice because we are issuing the securities only in global form.

For example, once we make a payment or give a notice to the legal holder, we have no further responsibility for the payment or notice even if that legal holder is required, under agreements with its participants or customers or by law, to pass it along to the indirect holders but does not do so. Similarly, we may want to obtain the approval of the holders to amend an indenture, to relieve us of the consequences of a default or of our obligation to comply with a particular provision of an indenture, or for other purposes. In such an event, we would seek approval only from the legal holders, and not the indirect holders, of the securities. Whether and how the legal holders contact the indirect holders is up to the legal holders.

Special Considerations For Indirect Holders

If you hold securities through a bank, broker or other financial institution, either in book-entry form because the securities are represented by one or more global securities or in street name, you should check with your own institution to find out:

- how it handles securities payments and notices;
- whether it imposes fees or charges;
- how it would handle a request for the holders' consent, if ever required;
- whether and how you can instruct it to send you securities registered in your own name so you can be a holder, if that is permitted in the future;
- how it would exercise rights under the securities if there were a default or other event triggering the need for holders to act to protect their interests; and
- if the securities are in book-entry form, how the depository's rules and procedures will affect these matters.

Global Securities

A global security is a security that represents one or any other number of individual securities held by a depository. Generally, all securities represented by the same global securities will have the same terms.

Each security issued in book-entry form will be represented by a global security that we issue to, deposit with and register in the name of a financial institution or its nominee that we select. The financial institution that we select for this purpose is called the depository. Unless we specify otherwise in the applicable prospectus supplement, The Depository Trust Company, New York, New York, known as DTC, will be the depository for all securities issued in book-entry form.

A global security may not be transferred to or registered in the name of anyone other than the depository, its nominee or a successor depository, unless special termination situations arise. We describe those situations below under “—Special Situations When A Global Security Will Be Terminated.” As a result of these arrangements, the depository, or its nominee, will be the sole registered owner and legal holder of all securities represented by a global security, and investors will be permitted to own only beneficial interests in a global security. Beneficial interests must be held by means of an account with a broker, bank or other financial institution that in turn has an account with the depository or with another institution that does. Thus, an investor whose security is represented by a global security will not be a legal holder of the security, but only an indirect holder of a beneficial interest in the global security.

If the prospectus supplement for a particular security indicates that the security will be issued as a global security, then the security will be represented by a global security at all times unless and until the global security is terminated. If termination occurs, we may issue the securities through another book-entry clearing system or decide that the securities may no longer be held through any book-entry clearing system.

Special Considerations For Global Securities

As an indirect holder, an investor's rights relating to a global security will be governed by the account rules of the investor's financial institution and of the depository, as well as general laws relating to securities transfers. We do not recognize an indirect holder as a holder of securities and instead deal only with the depository that holds the global security.

If securities are issued only as global securities, an investor should be aware of the following:

- an investor cannot cause the securities to be registered in his or her name, and cannot obtain non-global certificates for his or her interest in the securities, except in the special situations we describe below;

- an investor will be an indirect holder and must look to his or her own bank or broker for payments on the securities and protection of his or her legal rights relating to the securities, as we describe above;
- an investor may not be able to sell interests in the securities to some insurance companies and to other institutions that are required by law to own their securities in non-book-entry form;
- an investor may not be able to pledge his or her interest in the global security in circumstances where certificates representing the securities must be delivered to the lender or other beneficiary of the pledge in order for the pledge to be effective;
- the depositary's policies, which may change from time to time, will govern payments, transfers, exchanges and other matters relating to an investor's interest in the global security;
- we and any applicable trustee have no responsibility for any aspect of the depositary's actions or for its records of ownership interests in the global security, nor will we or any applicable trustee supervise the depositary in any way;
- the depositary may, and we understand that DTC will, require that those who purchase and sell interests in the global security within its book-entry system use immediately available funds, and your broker or bank may require you to do so as well; and
- financial institutions that participate in the depositary's book-entry system, and through which an investor holds its interest in the global security, may also have their own policies affecting payments, notices and other matters relating to the securities.

There may be more than one financial intermediary in the chain of ownership for an investor. We do not monitor and are not responsible for the actions of any of those intermediaries.

Special Situations When A Global Security Will Be Terminated

In a few special situations described below, a global security will terminate and interests in it will be exchanged for physical certificates representing those interests. After that exchange, the choice of whether to hold securities directly or in street name will be up to the investor. Investors must consult their own banks or brokers to find out how to have their interests in securities transferred to their own names, so that they will be direct holders. We have described the rights of holders and street name investors above.

Unless we provide otherwise in the applicable prospectus supplement, a global security will terminate when the following special situations occur:

- if the depositary notifies us that it is unwilling, unable or no longer qualified to continue as depositary for that global security and we do not appoint another institution to act as depositary within 90 days;
- if we notify any applicable trustee that we wish to terminate that global security; or
- if an event of default has occurred with regard to securities represented by that global security and has not been cured or waived.

The applicable prospectus supplement may also list additional situations for terminating a global security that would apply only to the particular series of securities covered by the applicable prospectus supplement. When a global security terminates, the depositary, and neither we nor any applicable trustee, is responsible for deciding the names of the institutions that will be the initial direct holders.

PLAN OF DISTRIBUTION

We may sell the securities covered hereby from time to time pursuant to underwritten public offerings, direct sales to the public, negotiated transactions, block trades or a combination of these methods. A distribution of the securities offered by this prospectus may also be effected through the issuance of derivative securities, including without limitation, warrants and subscriptions. We may sell the securities to or through underwriters or dealers, through agents, or directly to one or more purchasers. We may distribute securities from time to time in one or more transactions:

- at a fixed price or prices, which may be changed;

- at market prices prevailing at the time of sale;
- at prices related to such prevailing market prices;
- at varying prices determined at the time of sale; or
- at negotiated prices.

We may also sell equity securities covered by this registration statement in an “at the market offering” as defined in Rule 415 under the Securities Act. Such offering may be made into an existing trading market for such securities in transactions at other than a fixed price, either:

- on or through the facilities of The Nasdaq Global Market or any other securities exchange or quotation or trading service on which such securities may be listed, quoted or traded at the time of sale; and/or
- to or through a market maker otherwise than on The Nasdaq Global Market or such other securities exchanges or quotation or trading services.

Such at-the-market offerings, if any, may be conducted by financial institutions acting as principal or agent.

A prospectus supplement or supplements (and any related free writing prospectus that we may authorize to be provided to you) will describe the terms of the offering of the securities, including, to the extent applicable:

- the name or names of any underwriters, dealers or agents participating in the offering, if any;
- the purchase price of the securities sold by us to any underwriter or dealer and the net proceeds we expect to receive from the offering;
- any option, under which underwriters may purchase additional securities from us;
- any agency fees or underwriting discounts or commissions and other items constituting agents’ or underwriters’ compensation;
- any public offering price;
- any discounts or concessions allowed or reallocated or paid to dealers; and
- any securities exchange or market on which the securities may be listed.

Only underwriters named in the prospectus supplement are underwriters of the securities offered by the prospectus supplement.

If underwriters are used in the sale, they will acquire the securities for their own account and may resell the securities from time to time in one or more transactions at a fixed public offering price or at varying prices determined at the time of sale. The obligations of the underwriters to purchase the securities will be subject to the conditions set forth in the applicable underwriting agreement. We may offer the securities to the public through underwriting syndicates represented by managing underwriters or by underwriters without a syndicate. Subject to certain conditions, the underwriters will be obligated to purchase all of the securities offered by the prospectus supplement, other than securities covered by any option to purchase additional securities. Any public offering price and any discounts, commissions or concessions allowed or reallocated or paid to dealers may change from time to time. We may use underwriters with whom we have a material relationship. We will describe in the prospectus supplement, naming the underwriter, the nature of any such relationship.

We may sell securities directly or through agents we designate from time to time. We will name any agent involved in the offering and sale of securities, and we will describe any commissions and other compensation we will pay the agent in the prospectus supplement. Unless the prospectus supplement states otherwise, our agent will act on a best-efforts basis for the period of its appointment.

We may authorize agents or underwriters to solicit offers by certain types of institutional investors to purchase securities from us at the public offering price set forth in the prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. We will describe the conditions to these contracts and the commissions we must pay for solicitation of these contracts in the prospectus supplement.

We may provide agents and underwriters with indemnification against civil liabilities related to this offering, including liabilities under the Securities Act, or contribution with respect to payments that the agents or underwriters may make with respect to these liabilities. Agents and underwriters may engage in transactions with, or perform services for, us in the ordinary course of business.

All securities we may offer, other than common stock, will be new issues of securities with no established trading market. Any agents or underwriters may make a market in these securities, but will not be obligated to do so and may discontinue any market making at any time without notice. We cannot guarantee the liquidity of the trading markets for any securities. There is currently no market for any of the offered securities, other than our common stock which is listed on the on The Nasdaq Global Market. We have no current plans for listing of the debt securities, preferred stock, warrants or subscription rights on any securities exchange or quotation system; any such listing with respect to any particular debt securities, preferred stock, warrants or subscription rights will be described in the applicable prospectus supplement or other offering materials, as the case may be.

Any underwriter may engage in over-allotment, stabilizing transactions, short covering transactions and penalty bids in accordance with Regulation M under the Exchange Act. Over-allotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum. Short covering transactions involve purchases of the securities in the open market after the distribution is completed to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the securities originally sold by the dealer are purchased in a stabilizing or covering transaction to cover short positions. Those activities may cause the price of the securities to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time. These transactions may be effected on any exchange or over-the-counter market or otherwise.

Any agents and underwriters who are qualified market makers on The Nasdaq Global Market may engage in passive market making transactions in the securities on The Nasdaq Global Market in accordance with Rule 103 of Regulation M, during the business day prior to the pricing of the offering, before the commencement of offers or sales of the securities. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for such security; if all independent bids are lowered below the passive market maker's bid, however, the passive market maker's bid must then be lowered when certain purchase limits are exceeded. Passive market making may stabilize the market price of the securities at a level above that which might otherwise prevail in the open market and, if commenced, may be discontinued at any time.

In compliance with guidelines of the Financial Industry Regulatory Authority, Inc., or FINRA, the maximum compensation to be received by any FINRA member or independent broker dealer may not exceed 8% of the aggregate amount of the securities offered pursuant to this prospectus and any applicable prospectus supplement.

LEGAL MATTERS

Unless otherwise indicated in the applicable prospectus supplement, certain legal matters in connection with the offering and the validity of the securities offered by this prospectus, and any supplement thereto, will be passed upon for us by Morgan, Lewis & Bockius LLP. Additional legal matters may be passed upon for us or any underwriters, dealers or agents, by counsel that we will name in the applicable prospectus supplement.

EXPERTS

The consolidated financial statements of Proteon Therapeutics, Inc. appearing in Proteon Therapeutics, Inc. Annual Report (Form 10-K) for the year ended December 31, 2014 have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon, included therein, and incorporated herein by reference. Such consolidated financial statements are incorporated herein by reference in reliance upon such report, given on the authority of such firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

The consolidated financial statements of Proteon Therapeutics, Inc. appearing in Proteon Therapeutics, Inc. Annual Report (Form 10-K) for the year ended December 31, 2014 have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon, included therein, and incorporated herein by reference. Such consolidated financial statements are incorporated herein by reference in reliance upon such on the report, given on the authority of such firm as experts in auditing and accounting.

We file annual, quarterly and current reports, proxy statements and other information with the SEC. You may read and copy the registration statement, as well as any other document filed by us with the SEC, at the SEC's Public Reference Room at 100 F Street NE, Washington, D.C. 20549. You can also request copies of these documents by writing to the SEC and paying a fee for the copying cost. You may obtain information on the operation of the Public Reference Room by calling the SEC at (800) SEC-0330. The SEC maintains a website that contains reports, proxy statements and other information regarding issuers that file electronically with the SEC, including us. The address of the SEC website is www.sec.gov.

We maintain a website at www.proteontherapeutics.com. Information contained in or accessible through our website does not constitute a part of this prospectus.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to "incorporate by reference" information into this prospectus, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. The documents incorporated by reference into this prospectus contain important information that you should read about us. The information incorporated by reference is considered to be a part of this prospectus, and information in documents 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.

The following documents are incorporated by reference into this document:

- our Annual Report on Form 10-K for the fiscal year ended December 31, 2014 and filed with the SEC on March 20, 2015;
- our Quarterly Reports on Form 10-Q for the quarterly periods ended March 31, 2015, June 30, 2015 and September 30, 2015, filed with the SEC on May 13, 2015, August 13, 2015 and November 12, 2015, respectively;
- our Current Reports on Form 8-K filed with the SEC on March 20, 2015, March 27, 2015, April 2, 2015, May 13, 2015, June 2, 2015, June 5, 2015, July 13, 2015, July 22, 2015, August 13, 2015, October 19, 2015, November 2, 2015 and November 12, 2015; and
- the description of the our common stock contained in our registration statement on Form 8-A (No. 001-36694), filed with the SEC on October 16, 2014, including any amendments or reports filed for the purpose of updating such description.

We also incorporate by reference into this prospectus all documents (other than current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items) that are filed by us with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (i) after the date of the initial filing of the registration statement of which this prospectus forms a part and prior to effectiveness of the registration statement, or (ii) after the date of this prospectus but prior to the termination of the offering. These documents include periodic reports, such as Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q and Current Reports on Form 8-K, as well as proxy statements. Information in these documents updates and supplements the information provided in this prospectus. Any statements in these documents will automatically be deemed to modify and supersede any information in any document we previously filed with the SEC that is incorporated or deemed to be incorporated herein by reference to the extent that statements in the later filed document modify or replace such earlier statements.

We will provide to each person, including any beneficial owner, to whom a prospectus is delivered, without charge upon written or oral request, a copy of any or all of the documents that are incorporated by reference into this prospectus but not delivered with the prospectus, including exhibits which are specifically incorporated by reference into such documents. You should direct any requests for documents by writing us at 200 West Street, Waltham, Massachusetts 02451 or telephoning us at (781) 890-0102.

Any statement contained herein or in a document incorporated or deemed to be incorporated by reference into this document will be deemed to be modified or superseded for purposes of the document to the extent that a statement contained in this document or any other subsequently filed document that is deemed to be incorporated by reference into this document modifies or supersedes the statement.

DISCLOSURE OF COMMISSION'S POSITION ON INDEMNIFICATION FOR SECURITIES ACT LIABILITY

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers or persons controlling the Company pursuant to the foregoing provisions, we have been informed that in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable.

The information in this prospectus is not complete and may be changed. We may not sell these securities or accept an offer to buy 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 it is not soliciting offers to buy these securities in any state where such offer or sale is not permitted.

\$40,000,000



We have entered into a certain Sales Agreement, or sales agreement, with Cowen and Company, LLC, or Cowen, relating to shares of our common stock offered by this prospectus. In accordance with the terms of the sales agreement, we may offer and sell shares of our common stock having an aggregate offering price of up to \$40 million from time to time through Cowen.

Our common stock is quoted on The NASDAQ Global Market, or the Exchange, under the symbol "PRTO." The last reported sale price of our common stock on November 11, 2015 was \$14.74 per share.

Sales of our common stock, if any, under this prospectus may be made in sales deemed to be "at the market offerings" as defined in Rule 415 promulgated under the Securities Act of 1933, as amended, or the Securities Act, including sales made directly on or through the Exchange, the existing trading market for our common stock, sales made to or through a market maker other than on an exchange or otherwise, in negotiated transactions at market prices prevailing at the time of sale or at prices related to such prevailing market prices, and/or any other method permitted by law. Cowen is not required to sell any specific number or dollar amount of securities, but will act as a sales agent using commercially reasonable efforts consistent with its normal trading and sales practices, on mutually agreed terms between Cowen and us. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

The compensation to Cowen for sales of common stock sold pursuant to the sales agreement will be an amount equal to 3% of the gross proceeds of any shares of common stock sold under the sales agreement. In connection with the sale of the common stock on our behalf, Cowen will be deemed to be an "underwriter" within the meaning of the Securities Act and the compensation of Cowen will be deemed to be underwriting commissions or discounts. We have also agreed to provide indemnification and contribution to Cowen with respect to certain liabilities, including liabilities under the Securities Act or the Securities Exchange Act of 1934, as amended, or the Exchange Act. See section titled "Plan of Distribution" on page 10 of this prospectus.

Investing in our securities involves a high degree of risk. You should review carefully the risks and uncertainties described under the heading "Risk Factors" on page 2 of this prospectus and as updated in any applicable prospectus supplement and any related free writing prospectus, and under similar headings in the other documents that are 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 determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

Cowen and Company

_____, 2015

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ABOUT THIS PROSPECTUS

This prospectus relates to the offering of our common stock. Before buying any of the common stock that we are offering, we urge you to carefully read this prospectus, together with the information incorporated by reference as described under the headings “Where You Can Find More Information” and “Incorporation of Certain Information by Reference” in this prospectus, and any free writing prospectus or prospectus supplement that we have authorized for use in connection with this offering. These documents contain important information that you should consider when making your investment decision.

This prospectus describes the terms of this offering of common stock and also adds to and updates information contained in the documents incorporated by reference into this prospectus. To the extent there is a conflict between the information contained in this prospectus, on the one hand, and the information contained in any document incorporated by reference into this prospectus that was filed with the Securities and Exchange Commission, or SEC, before the date of this prospectus, on the other hand, you should rely on the information in this prospectus. If any statement in one of these documents is inconsistent with a statement in another document having a later date—for example, a document incorporated by reference into this prospectus—the statement in the document having the later date modifies or supersedes the earlier statement.

You should rely only on the information contained in or incorporated by reference in this prospectus and in any free writing prospectus or prospectus supplement that we have authorized for use in connection with this offering. We have not, and the sales agent has not, authorized anyone to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We are not, and the sales agent is 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 appearing in this prospectus, the documents incorporated by reference in this prospectus, and any free writing prospectus or prospectus supplement that we have authorized for use in connection with this offering, is accurate only as of the date of those respective documents. Our business, financial condition, results of operations and prospects may have changed since those dates.

Unless otherwise mentioned or unless the context indicates otherwise, as used in this prospectus, the terms “Proteon,” “the Company,” “we,” “us” and “our” refer to Proteon Therapeutics, Inc., a Delaware corporation, and, where appropriate, our consolidated subsidiary.

This prospectus and the information incorporated herein and therein by reference include trademarks, service marks and trade names owned by us or other companies. All trademarks, service marks and trade names included or incorporated by reference into this prospectus are the property of their respective owners.

PROSPECTUS SUMMARY

This summary highlights certain information about us, this offering and selected information contained elsewhere in or incorporated by reference into this prospectus. This summary is not complete and does not contain all of the information that you should consider before deciding whether to invest in our common stock. For a more complete understanding of our company and this offering, we encourage you to read and consider carefully the more detailed information in this prospectus, including the information incorporated by reference in this prospectus, and the information included in any free writing prospectus or prospectus supplement that we have authorized for use in connection with this offering, including the information under the heading “Risk Factors” in this prospectus on page 2 and in the documents incorporated by reference into this prospectus.

Proteon Therapeutics, Inc. is 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 (formerly PRT-201), is a recombinant human elastase that we are developing to improve AVF patency in patients with chronic kidney disease undergoing or preparing for hemodialysis, a lifesaving treatment that cannot be conducted without a functioning vascular access. We believe the data from our completed Phase 2 trial of vonapanitase in patients undergoing creation of an arteriovenous fistula, or AVF, support that a one-time, local application of vonapanitase during AVF surgical placement reduces AVF failure, thereby improving patient outcomes and reducing the burden on patients and the healthcare system. We are not aware of any approved preventative treatments to reduce the failure rate of AVFs. We enrolled the first patient in the first of two Phase 3 trials for vonapanitase in radiocephalic AVFs, our initial indication, in the third quarter of 2014 and subsequently completed patient enrollment in October 2015. We enrolled the first patient in our second Phase 3 trial in August 2015. Data from our first Phase 3 trial is expected in December 2016.

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.

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. The information contained in, or that can be accessed through, our website is not part of this prospectus.

THE OFFERING

| | |
|---------------------------------|---|
| Common stock offered by us | Shares of our common stock having an aggregate offering price of up to \$40 million. |
| Manner of offering | “At-the-market” offering that may be made from time to time through our sales agent, Cowen. See “Plan of Distribution” on page 10. |
| Use of proceeds | We currently intend to use the net proceeds from this offering primarily for research, development, manufacturing, and commercialization of product candidates, and for other general corporate purposes. See “Use of Proceeds” on page 3 of this prospectus. |
| Risk factors | Investing in our common stock involves significant risks. See “Risk Factors” on page 2 of this prospectus, and under similar headings in other documents incorporated by reference into this prospectus. |
| The NASDAQ Global Market Symbol | “PRTO” |

RISK FACTORS

Investing in our securities involves a high degree of risk. You should carefully review the risks and uncertainties described under the heading “Risk Factors” contained in any applicable prospectus supplement and any related free writing prospectus, and under similar headings in the other documents that are incorporated by reference into this prospectus, before deciding whether to purchase any of the securities being registered pursuant to the registration statement of which this prospectus is a part. The risks described in these documents are not the only ones we face, but those that we consider to be material. Each of the risk factors could adversely affect our business, operating results and financial condition, as well as adversely affect the value of an investment in our securities, and the occurrence of any of these risks might cause you to lose all or part of your investment. Moreover, the risks described are not the only ones that we face. Additional risks not presently known to us or that we currently believe are immaterial may also significantly impair our business operations. Please also read carefully the section below titled “Special Note Regarding Forward-Looking Statements.”

Additional Risks Related To This Offering

You will experience immediate and substantial dilution.

The offering price per share in this offering may exceed the net tangible book value per share of our common stock outstanding prior to this offering. Assuming that an aggregate of 2,713,704 shares of our common stock are sold at a price of \$14.74 per share, the last reported sale price of our common stock on the Exchange on November 11, 2015, for aggregate gross proceeds of \$40 million, and after deducting commissions and estimated offering expenses payable by us, you will experience immediate dilution of \$9.12 per share, representing the difference between our as adjusted net tangible book value per share as of September 30, 2015 after giving effect to this offering, on the one hand, and the assumed offering price, on the other. The exercise of outstanding stock options and warrants will result in further dilution of your investment. See the section titled “Dilution” below for a more detailed illustration of the dilution you would incur if you participate in this offering.

You may experience future dilution as a result of future equity offerings.

In order to raise additional capital, we may in the future offer additional shares of our common stock or other securities convertible into or exchangeable for our common stock at prices that may not be the same as the price per share in this offering. We may sell shares or other securities in any other offering at a price per share that is less than the price per share paid by investors in this offering, and investors purchasing shares or other securities in the future could have rights superior to existing stockholders. The price per share at which we sell additional shares of our common stock, or securities convertible or exchangeable into common stock, in future transactions may be higher or lower than the price per share paid by investors in this offering.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, the documents we file with the SEC that are incorporated by reference in this prospectus and any free writing prospectus or applicable prospectus supplement that we have authorized for use in connection with this offering contain “forward-looking statements” within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act that involve a number of risks and uncertainties. Although our forward-looking statements reflect the good faith judgment of our management, these statements can only be based on facts and factors currently known by us. Consequently, these forward-looking statements are inherently subject to risks and uncertainties, and actual results and outcomes may differ materially from results and outcomes discussed in the forward-looking statements.

Forward-looking statements can be identified by the use of forward-looking words such as “believes,” “expects,” “hopes,” “may,” “will,” “plan,” “intends,” “estimates,” “could,” “should,” “would,” “continue,” “seeks,” “pro forma,” or “anticipates,” or other similar words (including their use in the negative), or by discussions of future matters. These statements include but are not limited to statements under the captions “Business,” “Risk Factors” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and in other sections included in any applicable prospectus supplement or incorporated by reference from our Annual Report on Form 10-K and Quarterly Reports on Form 10-Q, as applicable, as well as our other filings with the SEC. You should be aware that the occurrence of any of the events discussed under the heading “Risk Factors” in any applicable prospectus supplement and any documents incorporated by reference herein or therein could substantially harm our business, operating results and financial condition and that if any of these events occurs, it could adversely affect the value of an investment in our securities.

The cautionary statements made in this prospectus are intended to be applicable to all related forward-looking statements wherever they may appear in this prospectus or in any free writing prospectus or prospectus supplement, or any documents incorporated by reference herein or therein. We urge you not to place undue reliance on these forward-looking statements, which speak only as of the date they are made. Except as required by law, we assume no obligation to update our forward-looking statements, even if new information becomes available in the future.

You should read this prospectus, the documents we file with the SEC that are incorporated by reference in this prospectus and any free writing prospectus or applicable prospectus supplement that we have authorized for use in connection with this offering completely and with the understanding that our actual future results may be materially different from what we expect. We qualify all of the forward-looking statements in the foregoing documents by these cautionary statements.

USE OF PROCEEDS

We may issue and sell shares of our common stock having aggregate sales proceeds of up to \$40 million from time to time. Because there is no minimum offering amount required as a condition to close this offering, the actual total public offering amount, commissions and proceeds to us, if any, are not determinable at this time. We estimate that the net proceeds from the sale of the shares of common stock that we are offering may be up to approximately \$38.8 million, after deducting Cowen’s commission and estimated offering expenses payable by us.

We currently intend to use the net proceeds from this offering primarily for research, development, manufacturing, and commercialization of product candidates, and for other general corporate purposes.

DILUTION

Our net tangible book value as of September 30, 2015 was approximately \$69 million, or \$4.19 per share. Net tangible book value per share is determined by dividing our total tangible assets, less total liabilities, by the number of shares of our common stock outstanding as of September 30, 2015. Dilution with respect to net tangible book value per share represents the difference between the amount per share paid by purchasers of shares of common stock in this offering and the net tangible book value per share of our common stock immediately after this offering.

After giving effect to the assumed sale of 2,713,704 shares of our common stock in this offering at an assumed offering price of \$14.74 per share, the last reported sale price of our common stock on the Exchange on November 11, 2015, and after deducting commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of September 30, 2015, 2015 would have been approximately \$107.8 million, or \$5.62 per share. This represents an immediate increase in net tangible book value of \$1.43 per share to existing stockholders and immediate dilution of \$9.12 per share to investors purchasing our common stock in this offering at the public offering price. The following table illustrates this dilution on a per share basis:

| | | |
|--|--------|---------|
| Assumed public offering price per share | | \$14.74 |
| Net tangible book value per share of as September 30 , 2015 | \$4.19 | |
| Increase in net tangible book value per share attributable to this offering | 1.43 | |
| As adjusted net tangible book value per share as of September 30, 2015, after giving effect to this offering | | 5.62 |
| Dilution per share to investors purchasing our common stock in this offering | | \$9.12 |

The above discussion and table are based on 16,479,508 shares outstanding as of September 30, 2015, and exclude as of that date:

- 1,800,262 shares of common stock issuable upon the exercise of stock options outstanding as of September 30, 2015, having a weighted average exercise price of \$7.00 per share;
- 639,895 shares of common stock reserved for future issuance under our 2014 Equity Incentive Plan;
- 299,127 shares of common stock reserved for future issuance under our 2014 Employee Stock Purchase Plan.

The table above assumes for illustrative purposes that an aggregate of 2,713,704 shares of our common stock are sold during the term of the sales agreement with Cowen at a price of \$14.74 per share, the last reported sale price of our common stock on The NASDAQ Global Market on November 11, 2015, for aggregate gross proceeds of \$40 million. The shares subject to the sales agreement with Cowen are being sold from time to time at various prices. An increase of \$1.00 per share in the price at which the shares are sold from the assumed offering price of \$14.74 per share shown in the table above, assuming all of our common stock in the aggregate amount of \$40 million during the term of the sales agreement with Cowen is sold at that price, would increase our adjusted net tangible book value per share after the offering to \$5.67 per share and would increase the dilution in net tangible book value per share to new investors in this offering to \$10.07 per share, after deducting commissions and estimated offering expenses payable by us. A decrease of \$1.00 per share in the price at which the shares are sold from the assumed offering price of \$14.74 per share shown in the table above, assuming all of our common stock in the amount of \$40 million during the term of the sales agreement with Cowen is sold at that price, would decrease our adjusted net tangible book value per share after the offering to \$5.56 per share and would decrease the dilution in net tangible book value per share to new investors in this offering to \$8.18 per share, after deducting commissions and estimated aggregate offering expenses payable by us. This information is supplied for illustrative purposes only and may differ based on the actual offering price and the actual number of shares offered.

To the extent that outstanding options or warrants outstanding as of September 30, 2015 have been or may be exercised or other shares issued, investors purchasing our common stock in this offering may experience further dilution. In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

DESCRIPTION OF CAPITAL STOCK

The description below of our capital stock and provisions of our amended and restated certificate of incorporation and amended and restated bylaws are summaries and are qualified by reference to the amended and restated certificate of incorporation, the amended and restated bylaws, and the applicable provisions of Delaware law.

General

Our amended and restated certificate of incorporation authorizes us to issue up to 100,000,000 shares of common stock, \$0.001 par value per share, and 10,000,000 shares of preferred stock, \$0.001 par value per share.

As of October 31, 2015, there were 16,484,508 shares of common stock outstanding, no shares of preferred stock outstanding, and no warrants for the purchase of shares of capital stock outstanding.

Common Stock

Voting rights. Each holder of our common stock is entitled to one vote for each share on all matters submitted to a vote of the stockholders, including the election of directors. Our stockholders do not have cumulative voting rights in the election of directors. An election of directors by our stockholders shall be determined by a plurality of votes cast by the stockholders entitled to vote on the election.

Dividends. Subject to preferences that may be applicable to any then outstanding preferred stock, holders of our common stock are entitled to receive dividends, if any, as may be declared from time to time by our board of directors out of legally available funds.

Liquidation. In the event of our liquidation, dissolution or winding up, holders of our common stock will be entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of all of our debts and other liabilities and the satisfaction of any liquidation preference granted to the holders of any then outstanding shares of preferred stock.

Rights and preferences. Holders of common stock have no preemptive, conversion or subscription rights and there are no redemption or sinking fund provisions applicable to the common stock. The rights, preferences and privileges of the holders of common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of preferred stock that we may designate in the future.

Fully paid and nonassessable. All of our outstanding shares of common stock are, and the shares of common stock to be issued in this offering, if any, will be, fully paid and nonassessable.

Preferred Stock

Under our amended and restated certificate of incorporation, our board of directors has the authority, without further action by the stockholders (unless such stockholder action is required by applicable law or the rules of any stock exchange or market on which our securities are then traded), to designate and issue up to 10,000,000 shares of preferred stock in one or more series, to establish from time to time the number of shares to be included in each such series, to fix the rights, preferences and privileges of the shares of each wholly unissued series and any qualifications, limitations or restrictions thereon and to increase or decrease the number of shares of any such series, but not below the number of shares of such series then outstanding.

We will fix the designations, voting powers, preferences and rights of the preferred stock of each series, as well as the qualifications, limitations or restrictions thereof, in a certificate of designation relating to that series. We will file as an exhibit to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of any certificate of designation that describes the terms of the series of preferred stock we are offering before the issuance of that series of preferred stock. This description will include:

- the title and stated value;
- the number of shares we are offering;
- the liquidation preference per share;
- the purchase price;

- the dividend rate, period and payment date and method of calculation for dividends;
- whether dividends will be cumulative or non-cumulative and, if cumulative, the date from which dividends will accumulate;
- the procedures for any auction and remarketing, if any;
- the provisions for a sinking fund, if any;
- the provisions for redemption or repurchase, if applicable, and any restrictions on our ability to exercise those redemption and repurchase rights;
- any listing of the preferred stock on any securities exchange or market;
- whether the preferred stock will be convertible into our common stock, and, if applicable, the conversion price, or how it will be calculated, and the conversion period;
- whether the preferred stock will be exchangeable into debt securities, and, if applicable, the exchange price, or how it will be calculated, and the exchange period;
- voting rights, if any, of the preferred stock;
- preemptive rights, if any;
- restrictions on transfer, sale or other assignment, if any;
- whether interests in the preferred stock will be represented by depositary shares;
- a discussion of any material U.S. federal income tax considerations applicable to the preferred stock;
- the relative ranking and preferences of the preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs;
- any limitations on the issuance of any class or series of preferred stock ranking senior to or on a parity with the series of preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs; and
- any other specific terms, preferences, rights or limitations of, or restrictions on, the preferred stock.

Delaware law provides that the holders of preferred stock will have the right to vote separately as a class (or, in some cases, as a series) on an amendment to our certificate of incorporation if the amendment would change the par value or, unless the certificate of incorporation provided otherwise, the number of authorized shares of the class or change the powers, preferences or special rights of the class or series so as to adversely affect the class or series, as the case may be. This right is in addition to any voting rights that may be provided for in the applicable certificate of designation.

Our board of directors may authorize the issuance of preferred stock with voting or conversion rights that could adversely affect the voting power or other rights of the holders of the common stock. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions and other corporate purposes, could, among other things, have the effect of delaying, deferring or preventing a change in our control that may otherwise benefit holders of our common stock and may adversely affect the market price of the common stock and the voting and other rights of the holders of common stock.

Warrants

As of October 31, 2015, we had no outstanding warrants to purchase shares of our capital stock.

Registration Rights

We agreed to provide certain registration rights to certain holders of our common stock pursuant to the terms of the Fourth Amended and Restated Investor's Rights Agreement, or IRA. We entered into the IRA in connection with the issuance of our Series D convertible preferred stock (which converted to common stock in our IPO) on May 13, 2014, and further amended the IRA on October 8, 2013 and February 5, 2014.

Anti-Takeover Effects of Provisions of Our Amended and Restated Certificate of Incorporation and Bylaws

Our amended and restated certificate of incorporation and amended and restated bylaws contain certain provisions that are intended to enhance the likelihood of continuity and stability in the composition of the board of directors and which may have the effect of delaying, deferring or preventing a future takeover or change in control of the Company unless such takeover or change in control is approved by the board of directors. These provisions include:

Classified Board. Our amended and restated certificate of incorporation provides that our board of directors will be divided into three classes of directors, with the classes as nearly equal in number as possible. At each annual meeting of the stockholders, a class of directors will be elected for a three-year term to succeed the directors of the same class whose terms are then expiring. As a result approximately one-third of our directors will be elected each year. The current term of office of the directors of Class I shall expire as of the annual meeting of the Company's stockholders taking place in fiscal year 2018; the initial term of office of the directors of Class II shall expire as of the annual meeting of the Company's stockholders taking place in fiscal year 2016; and the initial term of office of the directors of Class III shall expire as of the annual meeting of the Company's stockholders taking place in fiscal year 2017. The classification of directors will have the effect of making it more difficult for stockholders to change the composition of our board.

- Our Class I directors are Timothy Noyes, Garen Bohlin and John Freund;
- Our Class II directors are Hubert Birner, Dmitry Kobzyev, Gregory Phelps and Stuart Kingsley; and
- Our Class III directors are Brendan O'Leary, Tim Haines and Scott Canute.

Our amended and restated certificate of incorporation also provides that, subject to any rights of holders of preferred stock to elect additional directors under specified circumstances, the number of directors will be fixed exclusively pursuant to a resolution adopted by our board of directors. Any additional directorships resulting from an increase in the number of directors will be distributed among the three classes so that, as nearly as possible, each class shall consist of one third of the board of directors. Our board of directors currently has eight members.

Action by Written Consent; Special Meetings of Stockholders. Our amended and restated certificate of incorporation provides that stockholder action can be taken only at an annual or special meeting of stockholders and cannot be taken by written consent in lieu of a meeting. Our amended and restated certificate of incorporation and our amended and restated bylaws also provide that, except as otherwise required by law, special meetings of the stockholders can be called only by or at the direction of the board of directors pursuant to a resolution adopted by a majority of the total number of directors. Except as described above, stockholders are not permitted to call a special meeting or to require the board of directors to call a special meeting.

Removal of Directors. Our amended and restated certificate of incorporation provides that our directors may be removed only for cause by the affirmative vote of at least 75% of the voting power of our outstanding shares of capital stock, voting together as a single class and entitled to vote in the election of directors. This requirement of a supermajority vote to remove directors could enable a minority of our stockholders to prevent a change in the composition of our board.

Advance Notice Procedures. Our amended and restated bylaws establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to the board of directors. Stockholders at an annual meeting are only able to consider proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of the board of directors or by a stockholder who was a stockholder of record on the record date for the meeting, who is entitled to vote at the meeting and who has given our Secretary timely written notice, in proper form, of the stockholder's intention to bring that business before the meeting. Although the amended and restated bylaws do not give the board of directors the power to approve or disapprove stockholder nominations of candidates or proposals regarding other business to be conducted at a special or annual meeting, the amended and restated bylaws may have the effect of precluding the conduct of certain business at a meeting if the proper procedures are not followed or may discourage or deter a potential acquirer from conducting a solicitation of proxies to elect its own slate of directors or otherwise attempting to obtain control of the company.

Super Majority Approval Requirements. The Delaware General Corporation Law generally provides that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation's certificate of incorporation or bylaws, unless either a corporation's certificate of incorporation or bylaws requires a greater percentage. Our amended and restated certificate of incorporation and amended and restated bylaws provide that the affirmative vote of holders of at least 75% of the outstanding shares of capital stock, voting together as a single class and entitled to vote in the election of directors will be required to amend, alter, change or repeal the amended and restated bylaws and the amended and restated certificate of incorporation. This requirement of a supermajority vote to approve amendments to our amended and restated certificate of incorporation and amended and restated bylaws could enable a minority of our stockholders to exercise veto power over any such amendments.

Authorized but Unissued Shares. Our authorized but unissued shares of common stock and preferred stock will be available for future issuance without stockholder approval. These additional shares may be utilized for a variety of corporate purposes, including future public offerings to raise additional capital, corporate acquisitions and employee benefit plans. The existence of authorized but unissued shares of common stock and preferred stock could render more difficult or discourage an attempt to obtain control of a majority of our common stock by means of a proxy contest, tender offer, merger or otherwise.

Exclusive Forum. Our amended and restated certificate of incorporation provides that, subject to limited exceptions, the state or federal courts located in the State of Delaware will be the sole and exclusive forum for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or other employees to us or our stockholders, (iii) any action asserting a claim against us arising pursuant to any provision of the Delaware General Corporation Law, our amended and restated certificate of incorporation or our amended and restated bylaws, or (iv) any other action asserting a claim against us that is governed by the internal affairs doctrine. Any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock shall be deemed to have notice of and to have consented to the provisions of our amended and restated certificate of incorporation described above. Although we believe these provisions benefit us by providing increased consistency in the application of Delaware law for the specified types of actions and proceedings, the provisions may have the effect of discouraging lawsuits against our directors and officers. The enforceability of similar choice of forum provisions in other companies' certificates of incorporation has been challenged in legal proceedings, and it is possible that, in connection with one or more actions or proceedings described above, a court could find the choice of forum provisions contained in our amended and restated certificate of incorporation to be inapplicable or unenforceable.

Section 203 Of Delaware Law

We are subject to Section 203 of Delaware Law, or Section 203. In general, Section 203 prohibits a publicly-held Delaware corporation from engaging in a "business combination" with an "interested stockholder" for a three-year period following the time that this stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. A "business combination" includes, among other things, a merger, asset or stock sale or other transaction resulting in a financial benefit to the interested stockholder. An "interested stockholder" is a person who, together with affiliates and associates, owns, or did own within three years prior to the determination of interested stockholder status, 15% or more of the corporation's voting stock. Under Section 203, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions: before the stockholder became interested, the board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder; upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, shares owned by persons who are directors and also officers, and employee stock plans, in some instances; or at or after the time the stockholder became interested, the business combination was approved by the board of directors of the corporation and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder. A Delaware corporation may "opt out" of these provisions with an express provision in its original certificate of incorporation or an express provision in its certificate of incorporation or bylaws resulting from a stockholders' amendment approved by at least a majority of the outstanding voting shares. We have not opted out of these provisions. As a result, mergers or other takeover or change in control attempts of us may be discouraged or prevented.

Transfer Agent And Registrar

The transfer agent and registrar for our common stock is Computershare Trust Company, N.A. Its address is 250 Royall Street, Canton, Massachusetts 02021. The transfer agent for any series of preferred stock, debt securities or warrants that we may offer under this prospectus will be named and described in the prospectus supplement for that series.

NASDAQ Global Market Listing

Our common stock is listed on The NASDAQ Global Market under the symbol "PRTO."

PLAN OF DISTRIBUTION

We have entered into a sales agreement with Cowen, under which we may issue and sell from time to time up to \$40 million of our common stock through Cowen as our sales agent. Sales of our common stock, if any, will be made at market prices by any method that is deemed to be an “at the market offering” as defined in Rule 415 under the Securities Act, including sales made directly on The NASDAQ Global Market or any other trading market for our common stock, or sales to or through a market maker other than on an exchange. If authorized by us in writing, Cowen may also sell our shares of common stock by any other method permitted by law, including negotiated transactions, and Cowen may also purchase shares of our common stock as principal.

Cowen will offer our common stock subject to the terms and conditions of the sales agreement on a daily basis or as otherwise agreed upon by us and Cowen. We will designate the maximum amount of common stock to be sold through Cowen on a daily basis or otherwise determine such maximum amount together with Cowen. Subject to the terms and conditions of the sales agreement, Cowen will use its commercially reasonable efforts to sell on our behalf all of the shares of common stock requested to be sold by us. We may instruct Cowen not to sell common stock if the sales cannot be effected at or above the price designated by us in any such instruction. Cowen or we may suspend the offering of our common stock being made through Cowen under the sales agreement upon proper notice to the other party. Cowen and we each have the right, by giving written notice as specified in the sales agreement, to terminate the sales agreement in each party’s sole discretion at any time.

The aggregate compensation payable to Cowen as sales agent equals 3% of the gross sales price of the shares sold through it pursuant to the sales agreement. We have also agreed to reimburse Cowen up to \$50,000 of Cowen’s actual outside legal expenses incurred by Cowen in connection with this offering, and for certain other expenses, including Cowen’s FINRA counsel fees in an amount up to \$12,500. We estimate that the total expenses of the offering payable by us, excluding commissions payable to Cowen under the sales agreement, will be approximately \$38,105.

The remaining sales proceeds, after deducting any expenses payable by us and any transaction fees imposed by any governmental, regulatory, or self-regulatory organization in connection with the sales, will equal our net proceeds for the sale of such common stock.

Cowen will provide written confirmation to us following the close of trading on The NASDAQ Global Market on each day in which common stock is sold through it as sales agent under the sales agreement. Each confirmation will include the number of shares of common stock sold through it as sales agent on that day, the volume weighted average price of the shares sold, the percentage of the daily trading volume and the net proceeds to us.

We will report at least quarterly the number of shares of common stock sold through Cowen under the sales agreement, the net proceeds to us and the compensation paid by us to Cowen in connection with the sales of common stock.

Settlement for sales of common stock will occur, unless the parties agree otherwise, on the third business day that is also a trading day following the date on which any sales were made in return for payment of the net proceeds to us. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

In connection with the sales of our common stock on our behalf, Cowen may be deemed to be an “underwriter” within the meaning of the Securities Act, and the compensation paid to Cowen may be deemed to be underwriting commissions or discounts. We have agreed in the sales agreement to provide indemnification and contribution to Cowen against certain liabilities, including liabilities under the Securities Act. As sales agent, Cowen will not engage in any transactions that stabilizes our common stock.

Our common stock is listed on The NASDAQ Global Market and trades under the symbol “PRTO.” The transfer agent of our common stock is Computershare Trust Company, N.A.

Cowen and/or its affiliates have provided, and may in the future provide, various investment banking and other financial services for us for which services they have received and, may in the future receive, customary fees.

LEGAL MATTERS

The validity of the common stock offered by this prospectus will be passed upon for us by Morgan, Lewis & Bockius, LLP, Boston, Massachusetts. LeClairRyan, A Professional Corporation, Newark, New Jersey, is counsel for Cowen in connection with this offering.

EXPERTS

The consolidated financial statements of Proteon Therapeutics, Inc. appearing in Proteon Therapeutics, Inc. Annual Report (Form 10-K) for the year ended December 31, 2014 have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon, included therein, and incorporated herein by reference. Such consolidated financial statements are incorporated herein by reference in reliance upon such report, given on the authority of such firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus is part of a registration statement on Form S-3 we filed with the SEC under the Securities Act and does not contain all the information set forth in the registration statement. Whenever a reference is made in this prospectus to any of our contracts, agreements or other documents, the reference may not be complete and you should refer to the exhibits that are a part of the registration statement or the exhibits to the reports or other documents incorporated by reference therein. For further information with respect to us and the common stock we are offering under this prospectus, we refer you to the registration statement and the exhibits and schedules filed as a part of the registration statement. Neither we nor any agent, underwriter or dealer has authorized any person to provide you with different information. We are not making an offer of these securities in any state where the offer is not permitted. You should not assume that the information in this prospectus is accurate as of any date other than the date on the front page of this prospectus, regardless of the time of delivery of this prospectus or any sale of the common stock offered by this prospectus.

We file annual, quarterly and current reports, proxy statements and other information with the SEC. You may read and copy the registration statement, as well as any other document filed by us with the SEC, at the SEC's Public Reference Room at 100 F Street NE, Washington, D.C. 20549. You can also request copies of these documents by writing to the SEC and paying a fee for the copying cost. You may obtain information on the operation of the Public Reference Room by calling the SEC at (800) SEC-0330. The SEC maintains a website that contains reports, proxy statements and other information regarding issuers that file electronically with the SEC, including us. The address of the SEC website is www.sec.gov.

We maintain a website at www.proteontherapeutics.com. Information contained in or accessible through our website does not constitute a part of this prospectus.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to "incorporate by reference" information into this prospectus, which means that we can disclose important information to you by referring you to another document filed separately with the SEC. The documents incorporated by reference into this prospectus contain important information that you should read about us. The information incorporated by reference is considered to be a part of this prospectus, and information in documents 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.

The following documents are incorporated by reference into this document:

- our Annual Report on Form 10-K for the fiscal year ended December 31, 2014 and filed with the SEC on March 20, 2015;
- our Quarterly Reports on Form 10-Q for the quarterly periods ended March 31, 2015, June 30, 2015 and September 30, 2015, filed with the SEC on May 13, 2015, August 13, 2015 and November 12, 2015, respectively;
- our Current Reports on Form 8-K filed with the SEC on March 20, 2015, March 27, 2015, April 2, 2015, May 13, 2015, June 2, 2015, June 5, 2015, July 13, 2015, July 22, 2015, August 13, 2015, October 19, 2015, November 2, 2015 and November 12, 2015; and
- the description of the our common stock contained in our registration statement on Form 8-A (No. 001-36694), filed with the SEC on October 16, 2014, including any amendments or reports filed for the purpose of updating such description.

We also incorporate by reference into this prospectus all documents (other than current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items) that are filed by us with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (i) after the date of the initial filing of the registration statement of which this prospectus forms a part and prior to effectiveness of the registration statement, or (ii) after the date of this prospectus but prior to the termination of the offering. These documents include periodic reports, such as Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q and Current Reports on Form 8-K, as well as proxy statements. Information in these documents updates and supplements the information provided in this prospectus. Any statements in these documents will automatically be deemed to modify and supersede any information in any document we previously filed with the SEC that is incorporated or deemed to be incorporated herein by reference to the extent that statements in the later filed document modify or replace such earlier statements.

We will provide to each person, including any beneficial owner, to whom a prospectus is delivered, without charge upon written or oral request, a copy of any or all of the documents that are incorporated by reference into this prospectus but not delivered with the prospectus, including exhibits which are specifically incorporated by reference into such documents. You should direct any requests for documents by writing us at 200 West Street, Waltham, Massachusetts 02451 or telephoning us at (781) 890-0102.

Any statement contained herein or in a document incorporated or deemed to be incorporated by reference into this document will be deemed to be modified or superseded for purposes of the document to the extent that a statement contained in this document or any other subsequently filed document that is deemed to be incorporated by reference into this document modifies or supersedes the statement.

DISCLOSURE OF COMMISSION'S POSITION ON INDEMNIFICATION FOR SECURITIES ACT LIABILITY

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers or persons controlling the Company pursuant to the foregoing provisions, we have been informed that in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable.

\$40,000,000



Common Stock

PROSPECTUS

Cowen and Company

_____, 2015

PART II

INFORMATION NOT REQUIRED IN THE PROSPECTUS

Item 14. Other Expenses of Issuance and Distribution

The following table sets forth the estimated costs and expenses, other than underwriting discounts and commissions, payable by us in connection with the offering of the securities being registered.

| | Amount paid or to be paid |
|-------------------------------------|--------------------------------------|
| SEC registration fee | \$15,105 |
| FINRA filing fee | \$23,000 |
| Accounting fees and expenses | (1) |
| Legal fees and expenses | (1) |
| Transfer agent fees and expenses | (1) |
| Trustee fees and expenses | (1) |
| Printing and miscellaneous expenses | (1) |
| Total | (1) |

(1) These fees are calculated based on the securities offered and the number of issuances and accordingly cannot be estimated at this time.

Item 15. Indemnification of Officers and Directors

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.

The registrant maintains an insurance policy covering its officers and directors with respect to certain liabilities, including liabilities arising under the Securities Act or otherwise.

The underwriting agreement, if any, entered into with respect to an offering of securities registered hereunder will provide for indemnification by any underwriters of any offering, our directors and officers who sign the registration statement and our controlling persons for some liabilities, including liabilities arising under the Securities Act.

Item 16. Exhibits and Financial Statement Schedules

The exhibits required by Item 601 of Regulation S-K and Item 16 of this Registration Statement on Form S-3 are listed in the Exhibit Index immediately preceding the exhibits and are incorporated herein..

Item 17. Undertakings

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 of 1933;
 - (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 SEC pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than 20 percent 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 the undertakings set forth in paragraphs (1)(i), (1)(ii) and (1)(iii) above do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the SEC by the registrant pursuant to Section 13 or Section 15(d) of the Securities Exchange Act of 1934 that are incorporated by reference in this registration statement or is contained in a form of prospectus filed pursuant to Rule 424(b) that is part of this registration statement.

- (2) That, for the purpose of determining any liability under the Securities Act of 1933, 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.
 - (4) That, for the purpose of determining liability under the Securities Act of 1933 to any purchaser:
 - (i) 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
-

- (ii) 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.
- (5) That, for the purpose of determining liability of the registrant under the Securities Act of 1933 to any purchaser in the initial distribution of the securities, the undersigned registrant undertakes that in a primary offering of securities of the undersigned registrant pursuant to this registration statement, regardless of the underwriting method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, the undersigned registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser: (i) any preliminary prospectus or prospectus of the undersigned registrant relating to the offering required to be filed pursuant to Rule 424; (ii) any free writing prospectus relating to the offering prepared by or on behalf of the undersigned registrant or used or referred to by the undersigned registrant; (iii) the portion of any other free writing prospectus relating to the offering containing material information about the undersigned registrant or its securities provided by or on behalf of the undersigned registrant; and (iv) any other communication that is an offer in the offering made by the undersigned registrant to the purchaser.
- (6) That, for purposes of determining any liability under the Securities Act of 1933, each filing of the registrant's annual report pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the 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.
- (7) That for purposes of determining any liability under the Securities Act of 1933, (i) the information omitted from the form of prospectus filed as part of the registration statement in reliance upon Rule 430A and contained in the form of prospectus filed by the registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be a part of the registration statement as of the time it was declared effective; and (ii) each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.
- (8) To file an application for the purpose of determining the eligibility of the trustee to act under subsection (a) of Section 310 of the Trust Indenture Act in accordance with the rules and regulations prescribed by the SEC under Section 305(b)(2) of the Trust Indenture Act.

Insofar as indemnification for liabilities arising under the Securities Act of 1933 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 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, 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 Securities Act of 1933 and will be governed by the final adjudication of such issue.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, as amended, the registrant named below 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 12 day of November, 2015.

PROTEON THERAPEUTICS, INC.

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

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Timothy P. Noyes and George A. Eldridge, and each of them, as his or her true and lawful agent, proxy and attorney-in-fact, each acting alone, with full power of substitution and resubstitution, for him or her and in his or her name, place and stead, in any and all capacities, to (i) act on, sign, and file with the SEC any and all amendments (including post-effective amendments) to this registration statement together with all schedules and exhibits thereto, (ii) act on, sign and file such certificates, instruments, agreements and other documents as may be necessary or appropriate in connection therewith, (iii) act on and file any supplement to any prospectus included in this registration statement or any such amendment or any subsequent registration statement filed pursuant to Rule 462(b) under the Securities Act and (iv) take any and all actions which may be necessary or appropriate to be done, as fully for all intents and purposes as he or she might or could do in person, hereby approving, ratifying and confirming all that such agent, proxy and attorney-in-fact or any of his substitutes may lawfully do or cause to be done by virtue thereof.

Pursuant to the requirements of the Securities Act, as amended, this Registration Statement has been signed by the following persons in the capacities and on the dates indicated.

| Signatures | Title | Date |
|---|---|-------------------|
| <u>/s/ Timothy P. Noyes</u> Timothy P. Noyes | President, Chief Executive Officer and Director <i>(Principal Executive Officer)</i> | November 12, 2015 |
| <u>/s/ George A. Eldridge</u> George A. Eldridge | Senior Vice President, Chief Financial Officer, Treasurer and Secretary <i>(Principal Financial and Accounting Officer)</i> | November 12, 2015 |
| <u>Hubert Birner, Ph.D.</u> | Director | November __, 2015 |
| <u>/s/ Garen Bohlin</u> Garen Bohlin | Director | November 12, 2015 |
| <u>/s/ Scott Canute</u> Scott Canute | Director | November 12, 2015 |
| <u>/s/ John G. Freund, M.D.</u> John G. Freund, M.D. | Director | November 12, 2015 |

| | | |
|---|----------|-------------------|
| <u>/s/ Tim Haines</u> Tim Haines | Director | November 12, 2015 |
| <u>/s/ Stuart A. Kingsley</u> Stuart A. Kingsley | Director | November 12, 2015 |
| <u>/s/ Dmitry Kobzyev, Ph.D.</u> Dmitry Kobzyev, Ph.D. | Director | November 12, 2015 |
| <u>/s/ Brendan M. O'Leary, Ph.D.</u> Brendan M. O'Leary, Ph.D. | Director | November 12, 2015 |
| <u>/s/ Gregory D. Phelps</u> Gregory D. Phelps | Director | November 12, 2015 |

INDEX TO EXHIBITS

| Exhibit Number | Description of Document |
|-----------------------|---|
| 1.1* | Form of Underwriting Agreement |
| 3.1 | Sixth Amended and Restated Certificate of Incorporation of the Company (incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K filed on October 27, 2014 (File No. 001-36694)) |
| 3.2 | Amended and Restated Bylaws of the Company (incorporated by reference to Exhibit 3.2 to the Company's Current Report on Form 8-K filed on October 27, 2014 (File No. 001-36694)) |
| 4.1 | Fourth Amended and Restated Investors' Rights Agreement, dated May 13, 2014, between the Company and certain investors named therein (incorporated by reference to Exhibit 4.2 to the Company's Registration Statement on Form S-1 filed on September 16, 2014 (File No. 333-198777)) |
| 4.2 | Form of Common Stock Certificate (incorporated by reference to Exhibit 4.1 to Amendment No. 1 to the Company's Registration Statement on Form S-1 filed on October 7, 2014 (File No. 333-198777)) |
| 4.3* | Form of Preferred Stock Certificate |
| 4.4* | Form of Certificate of Designation of Preferred Stock |
| 4.5* | Form of Indenture, between the Company and one or more trustees to be named |
| 4.6* | Form of Common Stock Warrant Agreement and Warrant Certificate |
| 4.7* | Form of Preferred Stock Warrant Agreement and Warrant Certificate |
| 4.8* | Form of Debt Securities Warrant Agreement and Warrant Certificate |
| 5.1 | Opinion of Morgan, Lewis & Bockius LLP (filed herewith) |
| 10.1 | Sales Agreement dated as of November 12, 2015, between the Company and Cowen and Company, LLC (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed on November 12, 2015 (File No. 001-36694)) |
| 12.1* | Statement Regarding Computation of Ratios |
| 23.1 | Consent of Ernst & Young LLP, Independent Registered Public Accounting Firm (filed herewith) |
| 23.2 | Consent of Morgan, Lewis & Bockius LLP (included in Exhibit 5.1) |
| 24.1 | Power of Attorney (included on signature page) |
| 25.1* | Form T-1 Statement of Eligibility of Trustee under the Indenture |

* To be filed, if necessary, subsequent to the effectiveness of this Registration Statement by an amendment to this Registration Statement or incorporated by reference pursuant to a Current Report on Form 8-K in connection with an offering of securities, as appropriate.

Morgan, Lewis & Bockius LLP
One Federal Street
Boston, Massachusetts 02110-1726
Tel. +1.617.341.7700
Fax: +1.617.341.7701
www.morganlewis.com

Morgan Lewis

November 12, 2015

Proteon Therapeutics, Inc.
200 West Street
Waltham, MA 02451

Re: Registration Statement on Form S-3 of Proteon Therapeutics, Inc.

Ladies and Gentlemen:

We have acted as counsel to Proteon Therapeutics Inc., a Delaware corporation (the "Company"), in connection with the registration under the Securities Act of 1933, as amended (the "Act"), by a Registration Statement on Form S-3, dated November 12, 2015 (as may be amended, the "Registration Statement"), of an indeterminate amount of the Company's securities having an aggregate public offering price of up to \$150,000,000 to be offered from time to time pursuant to Rule 415 of the Act. Such securities may include (i) shares of the Company's common stock, par value \$0.001 per share (the "Common Stock"), (ii) shares of the Company's preferred stock, par value \$0.001 per share (the "Preferred Stock"), (iii) one or more series of the Company's debt securities (collectively, "Debt Securities"), (iv) warrants to purchase Common Stock, Preferred Stock or Debt Securities (the "Warrants" and, together with the Common Stock, Preferred Stock and Debt Securities, the "Securities"), and (v) any combination of two or more of the above Securities. The Registration Statement will be supplemented by one or more prospectus supplements.

The Debt Securities are to be issued pursuant to a senior indenture and/or a subordinated indenture, a form of which will be filed as an exhibit to the Registration Statement (the "Indenture") and is to be entered into, in each case, between the Company and a trustee (the "Trustee"). Each indenture may be supplemented, as applicable, in connection with the issuance of each series of Debt Securities by a supplemental indenture or other appropriate action of the Company creating such series. The Securities may be sold pursuant to an underwriting agreement, placement agency agreement, subscription agreement or other contract, which will be in substantially the form to be filed as an exhibit to a report filed pursuant to the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or an amendment to the Registration Statement. The Common Stock, Preferred Stock, Warrants and Debt Securities are to be issued in forms to be filed as exhibits to a report filed pursuant to the Exchange Act or an amendment to the Registration Statement.

As to all matters of fact (including factual conclusions and characterizations and descriptions of purpose, intention or other state of mind), we have relied, with your permission, entirely upon written actions by the board of directors of the Company and certificates of certain officers of the Company and have assumed, without independent inquiry, the accuracy of those certificates and written actions by the board of directors of the Company.

Almaty Astana Beijing Boston Brussels Chicago Dallas Dubai Frankfurt Harrisburg Hartford Houston London Los Angeles Miami Moscow
New York Orange County Paris Philadelphia Pittsburgh Princeton San Francisco Santa Monica Silicon Valley Singapore Tokyo Washington Wilmington

As counsel to the Company, in rendering the opinions hereinafter expressed, we have examined and relied upon originals or copies of such corporate records, agreements, documents and instruments as we have deemed necessary or advisable for purposes of this opinion, including (i) the Sixth Amended and Restated Certificate of Incorporation and Amended and Restated Bylaws of the Company, and (ii) the Registration Statement.

We have assumed:

- (i) the genuineness of all signatures, the conformity to the originals of all documents reviewed by us as copies, the authenticity and completeness of all original documents reviewed by us in original or copy form and the legal competence of each individual executing any document;
 - (ii) that any shares of Common Stock issued pursuant to the Registration Statement from time to time will not exceed the maximum authorized number of shares of Common Stock under the current Certificate of Incorporation of the Company, as the same may have been amended, minus that number of shares of Common Stock that may have been issued and are outstanding, or are reserved for issuance for other purposes, at such time;
 - (iii) that any shares of Preferred Stock issued pursuant to the Registration Statement from time to time will not exceed the maximum authorized number of shares of Preferred Stock under the current Certificate of Incorporation of the Company, as the same may have been amended, minus that number of shares of Preferred Stock that may have been issued and are outstanding, or are reserved for issuance for other purposes, at such time;
 - (iv) that at least \$2,500,000 will be advanced to the Company in payment of the consideration for the Debt Securities;
 - (v) that (1) the execution, delivery and performance by the Company of the applicable Indenture will not, and the execution, delivery and performance by the Company of any warrant agreement or other similar agreement entered into in connection with the issuance of any Securities will not, violate the laws of the jurisdiction of incorporation of the Company or any other applicable laws (excepting the internal, substantive laws of the State of New York and, to the limited extent provided herein, the Delaware General Corporation Law (the "DGCL")); and (2) the execution, delivery and performance by the Company of the applicable Indenture will not, and the execution, delivery and performance by the Company of any warrant agreement or other similar agreement entered into in connection with the issuance of any Securities will not, constitute a breach or violation of any agreement or instrument that is binding upon the Company; and
-

- (vi) that, at the time of each issuance and sale of the Securities, the Company will continue to be validly existing and in good standing under the laws of its jurisdiction of organization with the requisite corporate power and authority to issue and sell such Securities.

This opinion is limited solely to the DGCL, as applied by courts located in Delaware, and the internal, substantive laws of the State of New York as applied by courts located in New York without regard to choice of law, in each case to the extent that the same may apply to or govern the transactions contemplated by the Registration Statement. We express no opinion as to the effect of events occurring, circumstances arising, or changes of law becoming effective or occurring, after the date hereof on the matters addressed in this opinion.

Each opinion set forth below with respect to enforceability is subject to the following general qualifications:

- (a) enforceability may be limited by the effect of applicable bankruptcy, insolvency, reorganization, moratorium, marshaling, fraudulent conveyance or other similar laws and rules of law affecting the enforcement generally of creditors' or secured parties' rights and remedies;
 - (b) rights to indemnification and contribution may be limited by applicable law or equitable principles, and exculpatory provisions and waivers of the benefits of statutory provisions may be limited on public policy grounds;
 - (c) enforceability may be limited by general principles of equity, including without limitation concepts of materiality, reasonableness, good faith and fair dealing, and the possible unavailability of specific performance or injunctive relief and limitation of rights of acceleration, regardless of whether such enforceability is considered in a proceeding in equity or at law; and
 - (d) we express no opinion with respect to the enforceability of:
 - i. consents to, or restrictions upon, judicial relief or, except to the extent that such waivers or consents are made enforceable by New York General Obligations Law Section 5-1402 (as applied by a New York State court), jurisdiction or venue;
 - ii. advance waivers of claims, defenses, rights granted by law, or notice, opportunity for hearing, evidentiary requirements, statutes of limitation, trial by jury or at law, or other procedural rights;
 - iii. waivers of broadly or vaguely stated rights; and
 - iv. provisions for liquidated damages, default interest, late charges, monetary penalties, make-whole premiums or other economic remedies to the extent such provisions are deemed to constitute a penalty or a forfeiture.
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Based on such examination and subject to the foregoing, we are of the opinion that:

1. With respect to shares of Common Stock, when both (a) the Board of Directors of the Company or a duly constituted and acting committee thereof (such Board of Directors or committee being hereinafter referred to as the “Board”) has taken all necessary corporate action to approve the issuance and terms of the offering of shares of Common Stock and related matters, and (b) certificates representing the shares of Common Stock have been duly executed, countersigned, registered and delivered either (i) in accordance with the applicable definitive placement agency, underwriting, subscription or similar agreement approved by the Board, upon payment of the consideration therefor (not less than the par value of the Common Stock), (ii) upon the exercise of Warrants to purchase Common Stock and payment of the consideration therefor (not less than the par value of the Common Stock) provided for therein, or (iii) upon conversion or exercise of any other Security, in accordance with the terms of such Security or the instrument governing such Security providing for such conversion or exercise as approved by the Board, for the stated consideration (not less than the par value of the Common Stock), then the shares of Common Stock will be validly issued, fully paid and nonassessable.
 2. With respect to any particular series of shares of Preferred Stock, when both (a) the Board has taken all necessary corporate action to approve the issuance and terms of the shares of Preferred Stock, the terms of the offering thereof, and related matters, including the adoption of a certificate of designation relating to such Preferred Stock conforming to the DGCL (a “Certificate”) and the Certificate has been filed with the Secretary of State of the State of Delaware, and (b) certificates representing the shares of Preferred Stock have been duly executed, countersigned, registered and delivered either (i) in accordance with the applicable definitive placement agency, underwriting, subscription or similar agreement approved by the Board, upon payment of the consideration therefor (not less than the par value of the Preferred Stock), (ii) upon the exercise of Warrants to purchase Preferred Stock and payment of the consideration therefor (not less than the par value of the Preferred Stock) provided for therein, or (iii) upon conversion or exercise of any other Security, in accordance with the terms of such Security or the instrument governing such Security providing for such conversion or exercise as approved by the Board and for the stated consideration (not less than the par value of the Preferred Stock), then the shares of Preferred Stock will be validly issued, fully paid and nonassessable.
 3. With respect to the Warrants, when both (a) the Board has taken all necessary corporate action to approve the issuance and terms of the Warrants and related matters, and (b) the Warrants have been duly executed and delivered against payment therefor, pursuant to the applicable definitive placement agency, underwriting, subscription, warrant or similar agreement duly authorized, executed and delivered by the Company and any applicable warrant agent and the certificates for the Warrants have been duly executed and delivered by the Company and any applicable warrant agent, then the Warrants will constitute valid and binding obligations of the Company, enforceable against the Company in accordance with their terms.
 4. With respect to Debt Securities to be issued under the Indenture, when (a) the Trustee is qualified to act as Trustee under any Indenture, (b) the Trustee has duly authorized, validly executed and delivered the Indenture, (c) the applicable Indenture has been duly authorized and validly executed and delivered by the Company to the Trustee, (d) the applicable Indenture has been duly qualified under the Trust Indenture Act of 1939, as amended, (e) the Board has taken all necessary corporate action to approve the issuance and terms of such Debt Securities, the terms of the offering thereof and related matters, and (f) such Debt Securities have been duly executed, authenticated, issued and delivered in accordance with the provisions of the applicable Indenture, and the applicable definitive placement agency, underwriting, subscription or similar agreement approved by the Board, or upon the exercise of Warrants to purchase Debt Securities, upon payment of the consideration therefor provided for therein, such Debt Securities will constitute valid and binding obligations of the Company, enforceable against the Company in accordance with their terms and entitled to the benefits of the applicable Indenture.
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We hereby consent to the filing of this opinion as an exhibit to the Registration Statement and to the reference to this firm under the heading "Legal Matters" in the Prospectus included in the Registration Statement. In giving this consent, we do not admit that we are in the category of persons whose consent is required under Section 7 of the Act, or the rules and regulations of the Securities and Exchange Commission thereunder. In rendering this opinion, we are opining only as to the specific legal issues expressly set forth herein, and no opinion shall be inferred as to any other matter or matters. This opinion is intended solely for use in connection with the issuance and sale of the Securities subject to the Registration Statement and is not to be relied upon for any other purpose.

Very truly yours,

/s/ Morgan, Lewis & Bockius LLP

MORGAN, LEWIS & BOCKIUS LLP

Consent of Independent Registered Public Accounting Firm

We consent to the reference to our firm under the caption “Experts” in the Registration Statement (Form S-3) and related Prospectus of Proteon Therapeutics, Inc. for the registration of up to \$150,000,000 of debt securities, common stock, preferred stock, debt securities and warrants, and to the incorporation by reference therein of our report dated March 20, 2015, 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, 2014, filed with the Securities and Exchange Commission.

/s/ Ernst & Young LLP

Boston, Massachusetts
November 12, 2015