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Filed Pursuant to Rule 424(b)(5)
Registration No. 333-234414

PROSPECTUS SUPPLEMENT

(To Prospectus dated November 22, 2019)



Up To \$75,000,000 of Shares

Common Stock

We have entered into an Open Market Sale Agreement SM, or the sales agreement, with Jefferies LLC, or Jefferies, relating to the sale of shares of our common stock offered by this prospectus supplement and the accompanying prospectus. In accordance with the terms of the sales agreement, we may offer and sell shares of our common stock, \$0.00001 par value per share, from time to time having an aggregate offering price of up to \$75.0 million through Jefferies, acting as our sales agent.

Our common stock is traded on The Nasdaq Global Market under the symbol "PTGX." On November 26, 2019, the last reported sale price of our common stock was \$7.80 per share.

Sales of our shares, if any, under this prospectus supplement and the accompanying prospectus may be made in sales deemed to be an "at the market offering" as defined in Rule 415(a)(4) promulgated under the Securities Act of 1933, as amended, or the Securities Act. Jefferies 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 Jefferies and us. There is no arrangement for funds to be received in any escrow, trust or similar arrangement.

Jefferies will be entitled to compensation under the terms of the sales agreement at a fixed commission rate of up to 3.0% of the gross sales price per share sold under the sales agreement. See "Plan of Distribution" beginning on page S-13 for additional information regarding Jefferies' compensation. In connection with the sale of common stock on our behalf, Jefferies will be deemed to be an "underwriter" within the meaning of the Securities Act and the compensation of Jefferies will be deemed to be underwriting commissions or discounts. We have also agreed to provide indemnification to Jefferies against 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 S-13 of this prospectus supplement.

Investing in our securities involves a high degree of risk. See "Risk Factors" beginning on page S-8 of this prospectus supplement and under similar headings in the other documents that are incorporated by reference into this prospectus supplement.

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

We are an "emerging growth company" under the federal securities laws and are subject to reduced public company reporting requirements.

Jefferies

November 27, 2019

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ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part is this prospectus supplement, which describes the terms of this offering of common stock and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus. The second part, the accompanying prospectus dated November 22, 2019, including the documents incorporated by reference therein, provides more general information. Generally, when we refer to this prospectus, we are referring to both parts of this document combined. To the extent there is a conflict between the information contained in this prospectus supplement, on the one hand, and the information contained in the accompanying prospectus or in any document incorporated by reference that was filed with the Securities and Exchange Commission, or SEC, before the date of this prospectus supplement, on the other hand, you should rely on the information in this prospectus supplement. 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 supplement and the accompanying prospectus — the statement in the document having the later date modifies or supersedes the earlier statement.

We further note that the representations, warranties and covenants made by us in any agreement that is filed as an exhibit to any document that is incorporated by reference herein were made solely for the benefit of the parties to such agreement, including, in some cases, for the purpose of allocating risk among the parties to such agreements, and should not be deemed to be a representation, warranty or covenant to you. Moreover, such representations, warranties or covenants were accurate only as of the date when made. Accordingly, such representations, warranties and covenants should not be relied on as accurately representing the current state of our affairs.

We have not, and Jefferies has not, authorized anyone to provide you with information different than or inconsistent with the information contained in or incorporated by reference in this prospectus supplement, the accompanying prospectus or in any free writing prospectus that we have authorized for use in connection with this offering. We and Jefferies take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We are not, and Jefferies 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 supplement, the accompanying prospectus, the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, and in any free writing prospectus that we have authorized for use in connection with this offering, is accurate only as of the date of those respective documents, regardless of the time of delivery of those respective documents. Our business, financial condition, results of operations and prospects may have changed since those dates. You should read this prospectus supplement, the accompanying prospectus, the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, and any free writing prospectus that we have authorized for use in connection with this offering, in their entirety before making an investment decision. You should also read and consider the information in the documents to which we have referred you to in the section of this prospectus supplement entitled "Incorporation of Certain Information by Reference."

We are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted. The distribution of this prospectus supplement and the accompanying prospectus and the offering of our common stock in certain jurisdictions may be restricted by law. Persons outside the United States who come into possession of this prospectus supplement and the accompanying prospectus must inform themselves about, and observe any restrictions relating to, the offering of our common stock and the distribution of this prospectus supplement and the accompanying prospectus outside the United States. This prospectus supplement and the accompanying prospectus do not constitute, and may not be used in connection with, an offer to sell, or a solicitation of an offer to buy, any securities

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offered by this prospectus supplement and the accompanying prospectus by any person in any jurisdiction in which it is unlawful for such person to make such an offer or solicitation.

Except as otherwise indicated herein or as the context otherwise requires, references in this prospectus supplement, the accompanying prospectus and the information incorporated by reference herein and therein, to "Protagonist," "the company," "we," "us," "our" and similar references refer to Protagonist Therapeutics, Inc., a corporation under the laws of the State of Delaware.

This prospectus supplement and the information incorporated herein 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 supplement or any related free writing prospectus are the property of their respective owners.

PROSPECTUS SUPPLEMENT SUMMARY

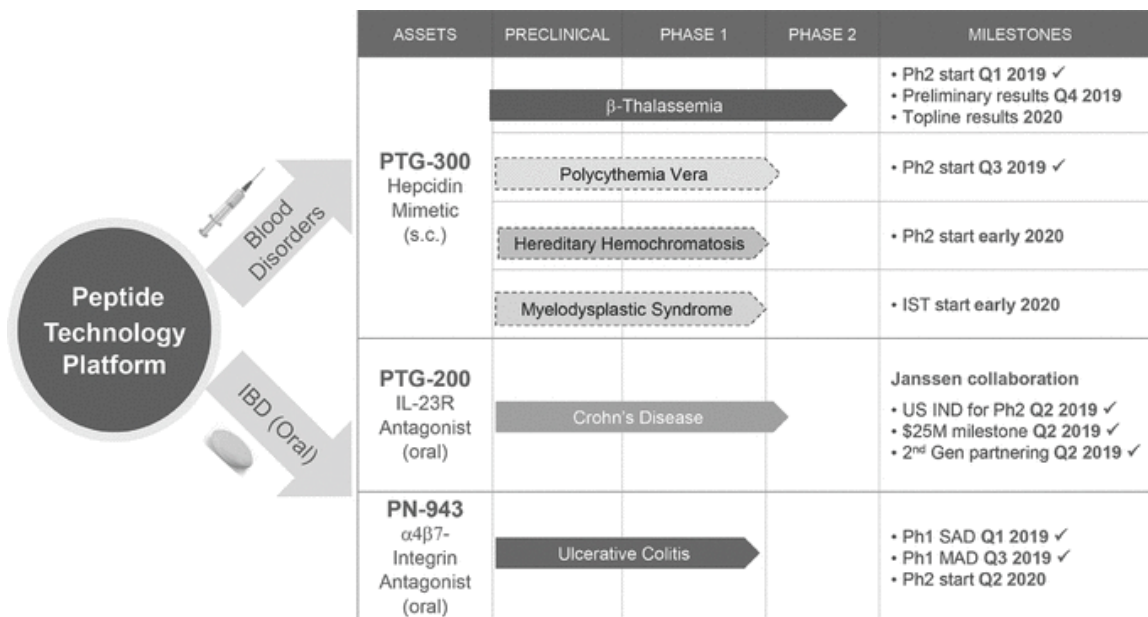
This summary highlights selected information contained elsewhere in this prospectus supplement or incorporated by reference herein and does not contain all of the information that you need to consider in making your investment decision. You should carefully read the entire prospectus supplement, the accompanying prospectus or related free writing prospectus, including the risks of investing in our securities discussed under the heading "Risk Factors" contained in this prospectus supplement, the accompanying prospectus or related free writing prospectus, and under similar headings in the other documents that are incorporated by reference into this prospectus supplement. You should also carefully read the information incorporated by reference into this prospectus supplement, including our financial statements and related notes incorporated by reference into this prospectus supplement and the accompanying prospectus, before making your investment decision.

Protagonist Therapeutics, Inc.

Overview

We are a clinical stage biopharmaceutical company developing peptide based product candidates to address significant unmet medical needs in hematology and gastroenterology.

Our Product Pipeline



In hematology, our most advanced clinical product candidate, PTG-300, is under development for the treatment of certain rare blood disorders characterized by ineffective erythropoiesis, excessive red blood cells or iron overload. PTG-300 is an injectable compound that mimics the effect of the natural hormone hepcidin, but with greater potency, solubility and stability. Hepcidin is a key hormone in regulating iron equilibrium and is critical to the proper development of red blood cells. We are currently developing PTG-300 for the treatment of ineffective erythropoiesis, chronic anemia and iron overload, with an initial focus on beta-thalassemia non-transfusion dependent and transfusion dependent patients where the primary endpoints are hemoglobin increases and transfusion burden reductions, respectively. PTG-300 has received an orphan drug designation from the U.S. Food and Drug Administration ("FDA") and European Union

regulatory authorities for the treatment of beta-thalassemia. The FDA has granted Fast Track designation to PTG-300 for the treatment of beta-thalassemia. In the first quarter of 2019, we began dosing patients in a global Phase 2 study of PTG-300 in beta-thalassemia. We expect to report preliminary results from this Phase 2 study in the fourth quarter of 2019 and top line results are expected in 2020. We initiated a Phase 2 study in polycythemia vera in the third quarter of 2019. We are working toward the initiation of both a clinical study of PTG-300 in the treatment of hereditary hemochromatosis and an investigator-sponsored study of PTG-300 in patients with myelodysplastic syndromes in early 2020.

In gastroenterology, our clinical stage product candidates, PTG-200 and PN-943, are potential first-in-class oral drugs currently in development for inflammatory bowel disease ("IBD"), a gastrointestinal ("GI") disease consisting primarily of ulcerative colitis ("UC") and Crohn's disease ("CD"), that block biological pathways currently targeted by marketed injectable antibody drugs. Our orally stable peptide approach offers targeted delivery to the GI tissue compartment. We believe that, compared to antibody drugs, these product candidates have the potential to provide improved safety due to minimal exposure in the blood, increased convenience and compliance due to oral delivery, and the opportunity for the earlier introduction of targeted therapy. As a result, if approved, they may transform the existing treatment paradigm for IBD.

PTG-200 is a potential first-in-class oral gut-restricted Interleukin-23 receptor antagonist for the treatment of IBD. We have entered into a worldwide license and collaboration agreement with Janssen Biotech, Inc. ("Janssen"), a Johnson & Johnson company, to co-develop and co-detail PTG-200 and any second-generation compounds, for all indications, including IBD. The agreement was amended on May 7, 2019 to expand the collaboration, triggering a \$25.0 million payment from Janssen received during the second quarter of 2019. In 2018, we completed a Phase 1 clinical study to evaluate the safety, pharmacokinetics and pharmacodynamics of PTG-200 in healthy volunteers. Janssen submitted a U.S. Investigational New Drug application for PTG-200 in CD during the second quarter of 2019, which took effect in July 2019. We initiated a Phase 2 clinical study in CD with Janssen in the fourth quarter of 2019.

PN-943 is a potential first-in-class oral, gut-restricted, alpha-4-beta-7 (" $\alpha4\beta7$ ") specific integrin antagonist. We developed PN-943 as a more potent oral gut-restricted $\alpha4\beta7$ backup compound to PTG-100, our first-generation oral gut-restricted $\alpha4\beta7$ inhibitor that was being developed for treatment of UC. In March 2018, we announced the discontinuation of a global Phase 2 clinical trial of PTG-100 in patients with moderate to severe UC due to futility following a planned interim analysis by an independent Data Monitoring Committee. In August 2018, we announced that a blinded re-read of endoscopies from the study by an independent contract research organization had demonstrated signals of clinical efficacy. A human error in the initial endoscopy reads by the original vendor which was characterized by an unusually high placebo effect led to the original futile outcome. In addition, a pre-specified blinded histopathology analysis of colon biopsies from the trial indicated dose-dependent high rates of histologic remission which supported the observations of clinical remission and endoscopy responses for PTG-100. During 2018 we replaced PTG-100 with PN-943 as a development candidate for the treatment of IBD based on an assessment of pre-clinical data from PN-943 suggesting that PN-943 is a more potent compound than PTG-100.

We completed a Phase 1 single ascending dose ("SAD") and multiple ascending dose ("MAD") clinical study of PN-943 in healthy volunteers to evaluate safety, pharmacokinetics and pharmacodynamics. We reported results of the SAD part of the study during the second quarter of 2019 and the MAD part of the study during the third quarter of 2019. The pharmacodynamic results indicated that the administration of PN-943 was safe and well tolerated, and results of target engagement were supportive of the higher potency of PN-943 as compared to PTG-100. We anticipate initiating a Phase 2 proof-of-concept study in UC in the second quarter of 2020.

Our clinical development programs are all derived from our proprietary discovery platform. Our platform enables us to engineer novel, structurally constrained peptides that retain key advantages of both oral small molecules and injectable antibody drugs, while overcoming many of their limitations as therapeutic agents. Importantly, constrained peptides can be designed to alleviate the fundamental instability inherent in

traditional peptides to allow different delivery forms, such as oral, subcutaneous, intravenous, and rectal. We continue to use our peptide technology platform to discover product candidates against targets in disease areas with significant unmet medical needs.

Janssen License and Collaboration Agreement

On May 26, 2017, we and Janssen, one of the Janssen Pharmaceutical Companies of Johnson & Johnson, entered into an exclusive license and collaboration agreement for the clinical development, manufacture and commercialization of PTG-200 worldwide for the treatment of CD and UC (the "Janssen License and Collaboration Agreement"), which was subsequently amended effective May 7, 2019. Janssen is a related party to us as Johnson & Johnson Innovation — JJDC, Inc., a significant stockholder of ours, and Janssen are both subsidiaries of Johnson & Johnson. During the third quarter of 2017, we received a non-refundable, upfront cash payment of \$50.0 million from Janssen. During the second quarter of 2019, we received a non-refundable cash payment of \$25.0 million upon execution of the amendment.

Company Information

Protagonist Pty Limited (Protagonist Australia) was incorporated in Australia in September 2001. We were incorporated under the laws of the State of Delaware in 2006, under the name Protagonist Therapeutics, Inc., and became the parent of Protagonist Australia pursuant to a transaction in which all of the issued and outstanding capital stock of Protagonist Australia was exchanged for shares of our common stock and Series A preferred stock. Our principal executive offices are located at 7707 Gateway Boulevard, Suite 140, Newark, California 94560. Our telephone number is (510) 474-0170. Our website address is www.protagonist-inc.com. The information contained in, or accessible through, our website does not constitute part of this prospectus supplement, should not be relied on in determining whether to make an investment decision, and the inclusion of our website address in this prospectus supplement is an inactive textual reference only.

The Protagonist logo and other trademarks or service marks of Protagonist Therapeutics, Inc. appearing in this prospectus supplement are the property of Protagonist Therapeutics, Inc. Other trademarks, service marks or trade names appearing in this prospectus supplement are the property of their respective owners. We do not intend our use or display of other companies' trade names, trademarks or service marks to imply a relationship with, or endorsement or sponsorship of us by, these other companies.

In addition, we are an "emerging growth company" as defined in the Jumpstart Our Business Startups Act, or the JOBS Act, enacted in April 2012, and therefore we intend to take advantage of certain exemptions from various public company reporting requirements, including not being required to have our internal control over financial reporting audited by our independent registered public accounting firm pursuant to Section 404(b) of the Sarbanes-Oxley Act of 2002, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements, exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and any golden parachute payments not previously approved.

THE OFFERING

Common Stock Offered By Us	Shares of our common stock having an aggregate offering price of up to \$75.0 million.
Manner of Offering	"At the market offering" that may be made from time to time through our sales agent, Jefferies. See "Plan of Distribution" on page S-13 of this prospectus supplement.
Use of Proceeds	We currently intend to use the net proceeds from this offering to fund clinical research and development of our clinical-stage assets, including the continued development of PTG-300, PTG-200 and PN-943, to advance our discovery programs and technology platform, and for working capital, capital expenditures and general corporate purposes. See "Use of Proceeds" on page S-10 of this prospectus supplement.
Risk Factors	Investing in our common stock involves significant risks. Please read the information contained in and incorporated by reference under the heading "Risk Factors" on page S-8 of this prospectus supplement and page 7 of the accompanying prospectus and under similar headings in the other documents that are filed after the date hereof and incorporated by reference into this prospectus supplement, together with the other information included in or incorporated by reference into this prospectus supplement and the accompanying prospectus, before deciding whether to invest in our common stock.
Nasdaq Global Market Symbol	PTGX

RISK FACTORS

Investing in our common stock involves a high degree of risk. Before deciding whether to invest in our common stock, you should consider carefully the risks and uncertainties described below and under the heading "Risk Factors" in the accompanying prospectus and under the heading "Risk Factors" contained in our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q, which are incorporated by reference into this prospectus supplement and the accompanying prospectus in their entirety, as updated or superseded by the risks and uncertainties described under similar headings in the other documents that are filed after the date hereof and incorporated by reference into this prospectus supplement, together with the other information in this prospectus supplement and the accompanying prospectus, the documents incorporated by reference and any free writing prospectus that we may authorize for use in connection with this offering. The risks described in these documents are not the only ones we face, but those that we consider to be material. There may be other unknown or unpredictable economic, business, competitive, regulatory or other factors that could have material adverse effects on our future results. Past financial performance may not be a reliable indicator of future performance, and historical trends should not be used to anticipate results or trends in future periods. If any of these risks actually occur, our business, financial condition, results of operations or cash flow could be seriously harmed. This could cause the trading price of our common stock to decline, resulting in a loss of all or part of your investment. Please also read carefully the section below titled "Forward-Looking Statements."

Additional Risks Related to This Offering

Management will have broad discretion as to the use of the proceeds from this offering, and may not use the proceeds effectively.

Because we have not designated the amount of net proceeds from this offering to be used for any particular purpose, our management will have broad discretion as to the application of the net proceeds from this offering and could use them for purposes other than those contemplated at the time of the offering. Our management may use the net proceeds for corporate purposes that may not improve our financial condition or market value.

You may 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 9,615,385 shares of our common stock are sold at a price of \$7.80 per share, the last reported sale price of our common stock on The Nasdaq Global Market on November 26, 2019, for aggregate gross proceeds of \$75.0 million, and after deducting commissions and estimated offering expenses payable by us, you would experience immediate dilution of \$3.24 per share, representing the difference between our as adjusted net tangible book value per share as of September 30, 2019 after giving effect to this offering and the assumed offering price. The exercise of outstanding stock options may result in further dilution of your investment. See the section titled "Dilution" below for a more detailed illustration of the dilution you may incur if you participate in this offering.

FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus, the documents incorporated by reference and any free writing prospectus, that we have authorized for use in connection with this offering, including the documents we incorporate by reference therein may contain forward-looking statements within the meaning of Section 27A of the Securities Act, and Section 21E of the Exchange Act, including statements regarding our future financial condition, business strategy and plans and objectives of management for future operations. Forward-looking statements include all statements that are not historical facts. In some cases, you can identify forward-looking statements by terminology such as "believe," "will," "may," "estimate," "continue," "anticipate," "intend," "should," "plan," "might," "approximately," "expect," "predict," "could," "potentially" or the negative of these terms or other similar expressions. Forward-looking statements appear in a number of places throughout this prospectus supplement, the accompanying prospectus, the documents incorporated by reference and any free writing prospectus that we have authorized for use in connection with this offering, including the documents we incorporate by reference therein may contain, and include statements regarding our intentions, beliefs, projections, outlook, analyses or current expectations concerning, among other things, the potential for our programs, the timing of our clinical trials, the potential for eventual regulatory approval and commercialization of our product candidates and our potential receipt of milestone payments and royalties under our collaboration agreement with Janssen, the potential outcome of any litigation or proceeding, future operating results or the ability to generate sales, income or cash flow are forward-looking statements.

Discussions containing these forward-looking statements may be found, among other places, in the section of this prospectus supplement under the heading "Risk Factors" and in the sections entitled "Business" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" incorporated by reference from our most recent Annual Report on Form 10-K and our Quarterly Reports on Form 10-Q, as well as any amendments thereto, filed with the SEC. These statements relate to future events or our future financial performance and involve known and unknown risks, uncertainties and other factors that could cause our actual results, levels of activity, performance or achievement to differ materially from those expressed or implied by these forward-looking statements. These statements reflect our current views with respect to future events and are based on assumptions and subject to risks and uncertainties. Given these risks and uncertainties, you should not place undue reliance on these forward-looking statements. We discuss in greater detail many of these risks under the heading "Risk Factors" in this prospectus supplement or free writing prospectus we may authorize for use in connection with a specific offering, and in our most recent Annual Report on Form 10-K and in our most recent Quarterly Report on Form 10-Q, as well as any amendments thereto reflected in subsequent filings with the SEC and in the other documents incorporated by reference herein, and elsewhere in this prospectus supplement. Also, these forward-looking statements represent our estimates and assumptions only as of the date of the document containing the applicable statement and, except as required by law, we undertake no obligation to update or revise publicly any forward-looking statements, whether as a result of new information, future events or otherwise.

In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this prospectus, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and investors are cautioned not to unduly rely upon these statements.

USE OF PROCEEDS

We may issue and sell shares of our common stock having aggregate sales proceeds of up to \$75.0 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 currently intend to use the net proceeds from this offering to fund clinical research and development of our clinical-stage assets, including the continued development of PTG-300, PTG-200 and PN-943, to advance our discovery programs and technology platform, and for working capital, capital expenditures and general corporate purposes. Pending these uses, we expect to invest the net proceeds in short-term, interest-bearing securities.

DILUTION

Our net tangible book value as of September 30, 2019 was approximately \$95.4 million, or \$3.50 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, 2019. 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 9,615,385 shares of our common stock in this offering at an assumed offering price of \$7.80 per share, the last reported sale price of our common stock on The Nasdaq Global Market on November 26, 2019, and after deducting estimated commissions and offering expenses payable by us, our as adjusted net tangible book value as of September 30, 2019 would have been approximately \$167.8 million, or \$4.56 per share. This represents an immediate increase in net tangible book value of \$1.06 per share to existing stockholders and immediate dilution of \$3.24 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	\$ 7.80
Net tangible book value per share of as September 30, 2019	\$ 3.50
Increase in net tangible book value per share attributable to this offering	\$ 1.06
As adjusted net tangible book value per share as of September 30, 2019, after giving effect to this offering	\$ 4.56
Dilution per share to new investors purchasing our common stock in this offering	\$ 3.24

The table above assumes for illustrative purposes that an aggregate of 9,615,385 shares of our common stock are sold during the term of the sales agreement with Jefferies at a price of \$7.80 per share, the last reported sale price of our common stock on The Nasdaq Global Market on November 26, 2019, for aggregate gross proceeds of \$75.0 million. The shares subject to the sales agreement with Jefferies may be 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 \$7.80 per share shown in the table above, assuming all of our common stock in the aggregate amount of \$75.0 million during the term of the sales agreement with Jefferies is sold at that price, would increase our adjusted net tangible book value per share after the offering to \$4.70 per share and would increase the dilution in net tangible book value per share to new investors in this offering to \$3.10 per share, after deducting commissions and estimated aggregate 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 \$7.80 per share shown in the table above, assuming all of our common stock in the aggregate amount of \$75.0 million during the term of the sales agreement with Jefferies is sold at that price, would decrease our adjusted net tangible book value per share after the offering to \$4.39 per share and would decrease the dilution in net tangible book value per share to new investors in this offering to \$3.41 per share, after deducting commissions and estimated 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.

The number of shares of our common stock to be outstanding after this offering is based on 27,206,447 shares of our common stock outstanding as of September 30, 2019 and excludes:

- 2,601,566 shares of common stock issuable upon the exercise of stock options issued and outstanding under our 2016 Equity Incentive Plan, or 2016 Plan, as of September 30, 2019, having a weighted average exercise price of \$16.11 per share;

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- 284,445 shares of common stock issuable upon the vesting of outstanding restricted stock units, under the 2016 Plan, as of September 30, 2019;
- an aggregate of 579,220 shares of common stock reserved for future issuance under the 2016 Plan, as of September 30, 2019;
- 470,000 shares of common stock issuable upon the exercise of stock options issued and outstanding under our 2018 Inducement Plan, or 2018 Plan, as of September 30, 2019, having a weighted average exercise price of \$7.66 per share;
- an aggregate of 280,000 shares of common stock reserved for future issuance under the 2018 Plan, as of September 30, 2019;
- 638,065 shares of common stock issuable upon the exercise of stock options issued and outstanding under our 2007 Equity Incentive Plan, or 2007 Plan, as of September 30, 2019, having a weighted average exercise price of \$3.18 per share;
- 577,993 shares of our common stock reserved for future issuance under our 2016 Employee Stock Purchase Plan, or 2016 ESPP, as of September 30, 2019;
- 2,750,000 shares of common stock issuable upon the exercise of warrants outstanding as of September 30, 2019, at a weighted average exercise price of \$12.50 per share; and
- 400,000 shares of common stock issuable upon the exercise of warrants outstanding as of September 30, 2019, at a weighted average exercise price of \$0.00001 per share.

To the extent that options, restricted stock units and warrants outstanding as of September 30, 2019 have been or may be exercised or settle, as applicable, 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.

PLAN OF DISTRIBUTION

We have entered into a sales agreement with Jefferies, under which we may offer and sell up to \$75,000,000 of our shares of common stock from time to time through Jefferies acting as agent. Sales of our shares of common stock, if any, under this prospectus supplement and the accompanying prospectus will be made by any method that is deemed to be an "at the market offering" as defined in Rule 415(a)(4) under the Securities Act.

Each time we wish to issue and sell our shares of common stock under the sales agreement, we will notify Jefferies of the number of shares to be issued, the dates on which such sales are anticipated to be made, any limitation on the number of shares to be sold in any one day and any minimum price below which sales may not be made. Once we have so instructed Jefferies, unless Jefferies declines to accept the terms of such notice, Jefferies has agreed to use its commercially reasonable efforts consistent with its normal trading and sales practices to sell such shares up to the amount specified on such terms. The obligations of Jefferies under the sales agreement to sell our shares of common stock are subject to a number of conditions that we must meet.

The settlement of sales of shares between us and Jefferies is generally anticipated to occur on the second trading day following the date on which the sale was made. Sales of our shares of common stock as contemplated in this prospectus supplement will be settled through the facilities of The Depository Trust Company or by such other means as we and Jefferies may agree upon. There is no arrangement for funds to be received in an escrow, trust or similar arrangement.

We will pay Jefferies a commission of up to 3.0% of the aggregate gross proceeds we receive from each sale of our shares of common stock. 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. In addition, we have agreed to reimburse Jefferies for the fees and disbursements of its counsel, payable upon execution of the sales agreement, in an amount not to exceed \$50,000, in addition to certain ongoing disbursements of its legal counsel. We estimate that the total expenses for the offering, excluding any commissions or expense reimbursement payable to Jefferies under the terms of the sales agreement, will be approximately \$310,000. The remaining sale proceeds, after deducting any other transaction fees, will equal our net proceeds from the sale of such shares.

Jefferies will provide written confirmation to us before the open on The Nasdaq Global Market on the day following each day on which our shares of common stock are sold under the sales agreement. Each confirmation will include the number of shares sold on that day, the aggregate gross proceeds of such sales and the proceeds to us.

In connection with the sale of our shares of common stock on our behalf, Jefferies will be deemed to be an "underwriter" within the meaning of the Securities Act, and the compensation of Jefferies will be deemed to be underwriting commissions or discounts. We have agreed to indemnify Jefferies against certain civil liabilities, including liabilities under the Securities Act. We have also agreed to contribute to payments Jefferies may be required to make in respect of such liabilities.

The offering of our shares of common stock pursuant to the sales agreement will terminate upon the earlier of (i) the sale of all shares of common stock subject to the sales agreement and (ii) the termination of the sales agreement as permitted therein. We and Jefferies may each terminate the sales agreement at any time upon ten trading days' prior notice.

This summary of the material provisions of the sales agreement does not purport to be a complete statement of its terms and conditions. A copy of the sales agreement is filed as an exhibit to a current report on Form 8-K filed under the Exchange Act, and incorporated by reference in this prospectus supplement.

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Jefferies and its affiliates may in the future provide various investment banking, commercial banking, financial advisory and other financial services for us and our affiliates, for which services they may in the future receive customary fees. In the course of its business, Jefferies may actively trade our securities for its own account or for the accounts of customers, and, accordingly, Jefferies may at any time hold long or short positions in such securities.

A prospectus supplement and the accompanying prospectus in electronic format may be made available on a website maintained by Jefferies, and Jefferies may distribute the prospectus supplement and the accompanying prospectus electronically.

LEGAL MATTERS

Cooley LLP has passed upon the validity of the common stock offered by this prospectus. Latham & Watkins LLP is counsel for Jefferies in connection with this offering.

EXPERTS

The financial statements incorporated in this prospectus supplement and elsewhere in the registration statement by reference to the [Annual Report on Form 10-K for the year ended December 31, 2018](#) have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus supplement and the accompanying prospectus are part of a registration statement we filed with the SEC. This prospectus supplement and the accompanying prospectus do not contain all of the information set forth in the registration statement and the exhibits to the registration statement. For further information with respect to us and the securities we are offering under this prospectus supplement, 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 supplement and the accompanying 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 supplement and the accompanying prospectus or any sale of the securities offered by this prospectus supplement and the accompanying prospectus.

We file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public at the SEC's website at <http://www.sec.gov>.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to "incorporate by reference" the information we file with it, which means that we can disclose important information to you by referring you to those documents instead of having to repeat the information in this prospectus supplement and the accompanying prospectus. The information incorporated by reference is considered to be part of this prospectus supplement and the accompanying prospectus, and later information that we file with the SEC will automatically update and supersede this information. We incorporate by reference the documents listed below and any future filings (including those made after the date of the initial filing of the registration statement of which this prospectus supplement and the accompanying prospectus are a part and prior to the effectiveness of such registration statement) we will make with the SEC under Sections 13(a), 13(c), 14, or 15(d) of the Exchange Act until the termination of the offering of the shares covered by this prospectus supplement and the accompanying prospectus (other than information furnished under Item 2.02 or Item 7.01 of Form 8-K):

- our [annual report on Form 10-K for the year ended December 31, 2018, filed with the SEC on March 12, 2019](#), including the information specifically incorporated by reference therein from our [definitive proxy statement on Schedule 14A, filed on April 26, 2019](#);
- [our Quarterly Report on Form 10-Q for the quarter ended March 31, 2019, filed with the SEC on May 8, 2019](#);
- [our Quarterly Report on Form 10-Q for the quarter ended June 30, 2019, filed with the SEC on August 7, 2019](#);
- [our Quarterly Report on Form 10-Q for the quarter ended September 30, 2019, filed with the SEC on November 6, 2019](#);
- our current reports on Form 8-K, filed with the SEC on [March 25, 2019](#), [May 8, 2019](#) (Item 1.01), [May 13, 2019](#), [May 29, 2019](#), [June 13, 2019](#) and [October 31, 2019](#); and
- [the description of our common stock set forth in our registration statement on Form 8-A, filed with the SEC on August 9, 2016, including any amendments thereto or reports filed for the purposes of updating this description](#).

You can request a copy of these filings, at no cost, by writing or telephoning us at the following address or telephone number:

Protagonist Therapeutics, Inc.
7707 Gateway Boulevard, Suite 140
Newark, California 94560
(510) 474-0170
Attn: Chief Financial Officer

PROSPECTUS



\$250,000,000

**Common Stock
Preferred Stock
Debt Securities
Warrants**

We may, from time to time, offer and sell up to \$250,000,000 of any combination of the securities described in this prospectus, either individually or in combination, at prices and on terms described in one or more supplements to this prospectus. We may also offer common stock or preferred stock upon conversion of debt securities, or common stock upon conversion of preferred stock, or common stock, preferred stock or debt securities upon exercise of warrants.

This prospectus describes some of the general terms that may apply to an offering of our securities. We will provide the specific terms of these offerings and securities in one or more supplements 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 the documents incorporated by reference, before buying any of the securities being offered.

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

Securities may be sold by us to or through underwriters or dealers, directly to purchasers or through agents designated from time to time. For additional information on the methods of sale, you should refer to the section entitled "Plan of Distribution" in this prospectus and in the applicable prospectus supplement. If any underwriters are involved in the sale of any securities with respect to which this prospectus is being delivered, the names of such underwriters and any applicable discounts or commissions and over-allotment options 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.

Our common stock is listed on the Nasdaq Global Market under the symbol "PTGX." On October 30, 2019, the last reported sale price of our common stock on the Nasdaq Global Market was \$12.44 per share. The applicable prospectus supplement will contain information, where applicable, as to other listings, if any, on the Nasdaq Global Market or other securities exchange of the securities covered by the 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 this prospectus on page 7 and in our most recent [Annual Report on Form 10-K](#) and [Quarterly Report on Form 10-Q](#) incorporated by reference into this prospectus, the applicable prospectus supplement and in any free writing prospectuses we have authorized for use in connection with a specific offering, 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.

We are an "emerging growth company" under the federal securities laws and are subject to reduced public company reporting requirements.

The date of this prospectus is November 22, 2019.

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You should rely only on the information contained in, or incorporated by reference into, this prospectus and the applicable prospectus supplement, along with the information contained in any free writing prospectuses we have authorized for use in connection with a specific offering. We have not authorized anyone to provide you with different information. We are not making an offer to sell or seeking an offer to buy securities under this prospectus or the applicable prospectus supplement and any related free writing prospectus in any jurisdiction where the offer or sale is not permitted. The information contained in this prospectus, the applicable prospectus supplement or any related free writing prospectus, and the documents incorporated by reference herein and therein, are accurate only as of their respective dates, regardless of the time of delivery of this prospectus, the applicable prospectus supplement or any related free writing prospectus, or any sale of a security.

ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement on Form S-3 that we filed with the Securities and Exchange Commission, or SEC, using a "shelf" registration process under the Securities Act of 1933, as amended, or the Securities Act. Under this shelf registration statement, we may sell from time to time in one or more offerings up to a total dollar amount of \$250,000,000 of common stock and preferred stock, various series of debt securities and/or warrants to purchase any of such securities, either individually or in combination with other securities as described in this prospectus. This prospectus provides you with a general description of the securities we may offer.

Each time we sell any type or series of securities under this prospectus, we will provide a prospectus supplement that will contain more 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. We may also add, update or change in a prospectus supplement or free writing prospectus any of the information contained in this prospectus or in the documents we have incorporated by reference into this prospectus. This prospectus, together with the applicable prospectus supplement, any related free writing prospectus and the documents incorporated by reference into this prospectus and the applicable prospectus supplement, will include all material information relating to the applicable offering. You should carefully read both this prospectus and the applicable prospectus supplement and any related free writing prospectus, together with the additional

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information described under "Where You Can Find More Information," before buying any of the securities being offered.

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

We have not authorized anyone to provide you with any information other than contained in, or incorporated by reference into, this prospectus and the applicable prospectus supplement, along with the information contained in any free writing prospectuses we have authorized for use in connection with a specific offering. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus is an offer to sell only the securities offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. You should not assume that the information contained in or incorporated by reference in this prospectus or any prospectus supplement or in any such free writing prospectus is accurate as of any date other than their respective dates. Our business, financial condition, results of operations and prospects may have changed since those dates.

This prospectus contains and incorporates by reference market data and industry statistics and forecasts that are based on independent industry publications and other publicly available information. Although we believe that these sources are reliable, we do not guarantee the accuracy or completeness of this information and we have not independently verified this information. Although we are not aware of any misstatements regarding the market and industry data presented in this prospectus and the documents incorporated herein by reference, these estimates involve risks and uncertainties and are subject to change based on various factors, including those 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. Accordingly, investors should not place undue reliance on this information.

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 section entitled "Where You Can Find More Information."

Except as otherwise indicated herein or as the context otherwise requires, references in this prospectus to "Protagonist," "the company," "we," "us," "our" and similar references refer to Protagonist Therapeutics, Inc., a corporation under the laws of the State of Delaware.

This prospectus and the information incorporated herein 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, any applicable prospectus supplement or any related free writing prospectus are the property of their respective owners.

PROSPECTUS SUMMARY

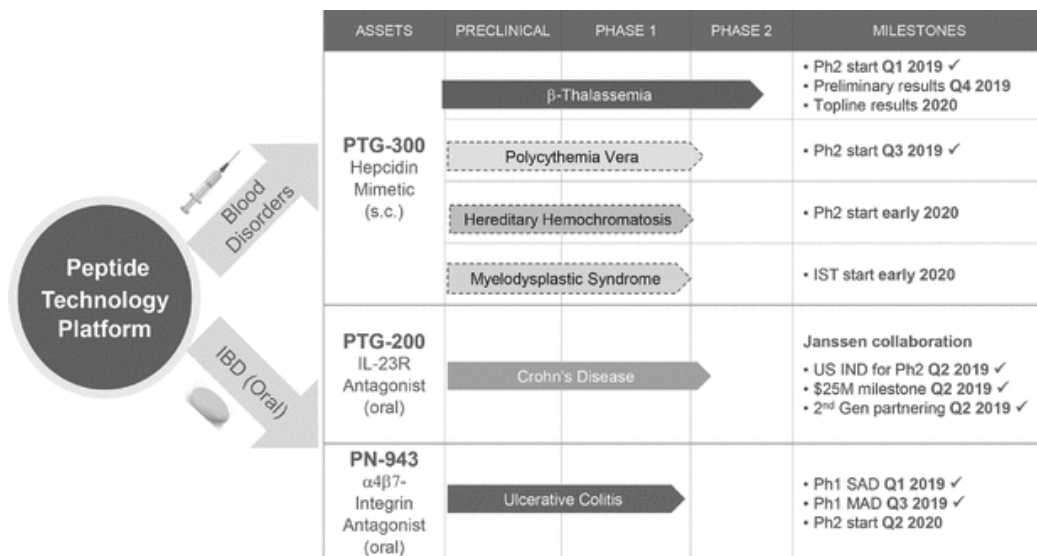
This summary highlights selected information contained elsewhere in this prospectus or incorporated by reference herein and does not contain all of the information that you need to consider in making your investment decision. You should carefully read the entire prospectus, the applicable prospectus supplement and any related free writing prospectus, including the risks of investing in our securities discussed under the heading "Risk Factors" contained in this prospectus, 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 financial statements and related notes, and the exhibits to the registration statement of which this prospectus is a part, before making your investment decision.

Protagonist Therapeutics, Inc.

Overview

We are a clinical-stage biopharmaceutical company developing peptide-based product candidates to address significant unmet medical needs in hematology and gastroenterology.

Our Product Pipeline



In hematology, our most advanced clinical product candidate, PTG-300, is under development for the treatment of certain rare blood disorders characterized by ineffective erythropoiesis, excessive red blood cells or iron overload. PTG-300 is an injectable compound that mimics the effect of the natural hormone hepcidin, but with greater potency, solubility and stability. Hepcidin is a key hormone in regulating iron equilibrium and is critical to the proper development of red blood cells. We are currently developing PTG-300 for the treatment of ineffective erythropoiesis, chronic anemia and iron overload, with an initial focus on beta-thalassemia non-transfusion dependent and transfusion dependent patients where the primary endpoints are hemoglobin increases and transfusion burden reductions, respectively. PTG-300 has received an orphan drug designation from the U.S. Food and Drug Administration ("FDA") and European Union ("EU") regulatory authorities for the treatment of beta-thalassemia. The FDA has granted Fast Track designation to PTG-300 for the treatment of beta-thalassemia. In the first quarter of 2019, we began dosing patients in a global Phase 2 study of PTG-300 in beta-thalassemia. We expect to report preliminary results from this Phase 2 study in the

fourth quarter of 2019 and top line results are expected in 2020. We initiated a Phase 2 study in polycythemia vera ("PV") in the third quarter of 2019. We are working toward the initiation of both a clinical study of PTG-300 in the treatment of hereditary hemochromatosis ("HH") and an investigator-sponsored study of PTG-300 in patients with myelodysplastic syndromes ("MDS") in early 2020.

In gastroenterology our clinical stage product candidates, PTG-200 and PN-943, are potential first-in-class oral drugs currently in development for inflammatory bowel disease ("IBD"), a gastrointestinal ("GI") disease consisting primarily of ulcerative colitis ("UC") and Crohn's disease ("CD"), that block biological pathways currently targeted by marketed injectable antibody drugs. Our orally stable peptide approach offers targeted delivery to the GI tissue compartment. We believe that, compared to antibody drugs, these product candidates have the potential to provide improved safety due to minimal exposure in the blood, increased convenience and compliance due to oral delivery, and the opportunity for the earlier introduction of targeted therapy. As a result, if approved, they may transform the existing treatment paradigm for IBD.

PTG-200 is a potential first-in-class oral gut-restricted Interleukin-23 receptor ("IL-23R") antagonist for the treatment of IBD. We have entered into a worldwide license and collaboration agreement with Janssen Biotech, Inc. ("Janssen"), a Johnson & Johnson company, to co-develop and co-detail PTG-200 and any second-generation compounds, for all indications, including IBD. The agreement was amended on May 7, 2019 to expand the collaboration, triggering a \$25.0 million payment from Janssen received during the second quarter of 2019. In 2018, we completed a Phase 1 clinical study to evaluate the safety, pharmacokinetics and pharmacodynamics of PTG-200 in healthy volunteers. Janssen submitted a U.S. Investigational New Drug application ("IND") for PTG-200 in CD during the second quarter of 2019, which took effect in July 2019. We initiated a Phase 2 clinical study in CD with Janssen in the fourth quarter of 2019.

PN-943 is a potential first-in-class oral, gut-restricted, alpha-4-beta-7 (" $\alpha4\beta7$ ") specific integrin antagonist. We developed PN-943 as a more potent oral gut-restricted $\alpha4\beta7$ backup compound to PTG-100, our first-generation oral gut-restricted $\alpha4\beta7$ inhibitor that was being developed for treatment of UC. In March 2018, we announced the discontinuation of a global Phase 2 clinical trial of PTG-100 in patients with moderate to severe UC due to futility following a planned interim analysis by an independent Data Monitoring Committee. In August 2018, we announced that a blinded re-read of endoscopies from the study by an independent contract research organization had demonstrated signals of clinical efficacy. A human error in the initial endoscopy reads by the original vendor which was characterized by an unusually high placebo effect led to the original futile outcome. In addition, a pre-specified blinded histopathology analysis of colon biopsies from the trial indicated dose-dependent high rates of histologic remission which supported the observations of clinical remission and endoscopy responses for PTG-100. During 2018 we replaced PTG-100 with PN-943 as a development candidate for the treatment of IBD based on an assessment of pre-clinical data from PN-943 suggesting that PN-943 is a more potent compound than PTG-100.

We completed a Phase 1 single ascending dose ("SAD") and multiple ascending dose ("MAD") clinical study of PN-943 in healthy volunteers to evaluate safety, pharmacokinetics and pharmacodynamics. We reported results of the SAD part of the study during the second quarter of 2019 and the MAD part of the study during the third quarter of 2019. The pharmacodynamic results indicated that the administration of PN-943 was safe and well tolerated, and results of target engagement were supportive of the higher potency of PN-943 as compared to PTG-100. We anticipate initiating a Phase 2 proof-of-concept study in UC in the second quarter of 2020.

Our clinical development programs are all derived from our proprietary discovery platform. Our platform enables us to engineer novel, structurally constrained peptides that retain key advantages of both oral small molecules and injectable antibody drugs, while overcoming many of their limitations as therapeutic agents. Importantly, constrained peptides can be designed to alleviate the fundamental

instability inherent in traditional peptides to allow different delivery forms, such as oral, subcutaneous, intravenous, and rectal. We continue to use our peptide technology platform to discover product candidates against targets in disease areas with significant unmet medical needs.

Janssen License and Collaboration Agreement

On May 26, 2017, we and Janssen, one of the Janssen Pharmaceutical Companies of Johnson & Johnson, entered into an exclusive license and collaboration agreement for the clinical development, manufacture and commercialization of PTG-200 worldwide for the treatment of CD and UC (the "Janssen License and Collaboration Agreement"), which was subsequently amended effective May 7, 2019. Janssen is a related party to us as Johnson & Johnson Innovation—JJDC, Inc., a significant stockholder of ours, and Janssen are both subsidiaries of Johnson & Johnson. During the third quarter of 2017, we received a non-refundable, upfront cash payment of \$50.0 million from Janssen. During the second quarter of 2019, we received a non-refundable cash payment of \$25.0 million due upon execution of the amendment.

Company Information

Protagonist Pty Limited (Protagonist Australia) was incorporated in Australia in September 2001. We were incorporated under the laws of the State of Delaware in 2006, under the name Protagonist Therapeutics, Inc., and became the parent of Protagonist Australia pursuant to a transaction in which all of the issued and outstanding capital stock of Protagonist Australia was exchanged for shares of our common stock and Series A preferred stock. Our principal executive offices are located at 7707 Gateway Boulevard, Suite 140, Newark, California 94560. Our telephone number is (510) 474-0170. Our website address is www.protagonist-inc.com. The information contained in, or accessible through, our website does not constitute part of this prospectus, should not be relied on in determining whether to make an investment decision, and the inclusion of our website address in this prospectus is an inactive textual reference only.

The Protagonist logo and other trademarks or service marks of Protagonist Therapeutics, Inc. appearing in this prospectus are the property of Protagonist Therapeutics, Inc. Other trademarks, service marks or trade names appearing in this prospectus are the property of their respective owners. We do not intend our use or display of other companies' trade names, trademarks or service marks to imply a relationship with, or endorsement or sponsorship of us by, these other companies.

Risks Associated with our Business

Our business is subject to numerous risks, as described under the heading "Risk Factors" contained in the applicable prospectus supplement and in any free writing prospectuses we have authorized for use in connection with a specific offering, and under similar headings in the documents that are incorporated by reference into this prospectus.

THE SECURITIES WE MAY OFFER

We may offer shares of our common stock and preferred stock, various series of debt securities and/or warrants to purchase any of such securities, either individually or in combination, with a total dollar amount up to \$250,000,000 from time to time under this prospectus, together with the applicable prospectus supplement and any related free writing prospectus, at prices and on terms to be determined at the time of any offering. We may also offer common stock, preferred stock and/or debt securities upon the exercise of warrants. 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;
- original issue discount;
- rates and times of payment of interest or dividends;
- redemption, conversion, exercise, exchange or sinking fund terms;
- ranking;
- restrictive covenants;
- voting or other rights;
- conversion or exchange prices or rates 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; and
- a discussion of material United States federal income tax considerations, if any.

The applicable prospectus supplement and any related free writing prospectus that we may authorize to be provided to you may also add, update or change any of the information contained in this prospectus or in the 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 to or through agents, underwriters or dealers. We, and our agents, underwriters or dealers reserve the right to accept or reject all or part of any proposed purchase of securities. If we do offer securities to or through agents, underwriters or dealers, we will include in the applicable prospectus supplement:

- the names of those agents, underwriters or dealers;
- applicable fees, discounts and commissions to be paid to them;
- details regarding over-allotment options, if any; and
- the net proceeds to us, if any.

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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. Under our amended and restated certificate of incorporation, or certificate of incorporation, and amended and restated bylaws, or bylaws, our stockholders do not have cumulative voting rights. Because of this, the holders of a majority of the shares of common stock entitled to vote in any election of directors can elect all of the directors standing for election, if they should so choose. Subject to preferences that may be applicable to any then-outstanding preferred stock, holders of common stock are entitled to receive ratably those 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 common stock are 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. In this prospectus, we have summarized certain general features of the 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. Our board of directors will determine the designations, voting powers, preferences and rights of the preferred stock, 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, or the designation of such series, any or all of which may be greater than the rights of our common stock. Convertible preferred stock will be convertible into our common stock or exchangeable for other securities. Conversion may be mandatory or at your option and would be at prescribed conversion rates.

If we sell any series of preferred stock under this prospectus, we will fix the designations, voting powers, preferences and rights of such series of preferred stock, as well as the qualifications, limitations or restrictions thereof, in the 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 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 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 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

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instrument governing the debt, to all of our senior indebtedness. Convertible or exchangeable debt securities will be convertible into or exchangeable for our common stock or our other securities. Conversion or exchange may be mandatory or optional (at our option or the holders' option) and would be at prescribed conversion or exchange rates.

Any debt securities issued under this prospectus 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 under "Description of 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 indenture and any supplemental 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 in combination with common stock, preferred stock and/or debt securities offer by any prospectus supplement. In this prospectus, we have summarized certain general features of the warrants under "Description of Warrants." 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 particular series of warrants being offered, as well as any warrant agreements and warrant certificates, as applicable, that contain the terms of the warrants. We have filed forms of the warrant agreements and forms of warrant certificates containing the terms of the warrants that may be offered as exhibits to the registration statement of which this prospectus is a part. 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 and/or the warrant agreement and warrant certificate, as applicable, that contain the terms of the particular series of warrants we are offering, and any supplemental agreements, before the issuance of such warrants.

Any warrants issued under this prospectus may be evidenced by warrant certificates. Warrants also 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.

Use of Proceeds

Except as described in any applicable prospectus supplement or in any free writing prospectus we have authorized for use in connection with a specific offering, we currently intend to use the net proceeds from the sale of the shares of our securities offered by us hereunder, if any, for working capital, capital expenditures and other general corporate purposes. See "Use of Proceeds" in this prospectus.

RISK FACTORS

Investing in our securities involves a high degree of risk. Before deciding whether to invest in our securities, you should consider carefully the risks and uncertainties described under the heading "Risk Factors" contained in the applicable prospectus supplement and any related free writing prospectus, and discussed under the section entitled "Risk Factors" contained in our most recent [Annual Report on Form 10-K](#) and in our most recent [Quarterly Report on Form 10-Q](#), as well as any amendments thereto reflected in subsequent filings with the SEC, which are incorporated by reference into this prospectus in their entirety, together with other information in this prospectus, the documents incorporated by reference and any free writing prospectus that we may authorize for use in connection with this offering. The risks described in these documents are not the only ones we face, but those that we consider to be material. There may be other unknown or unpredictable economic, business, competitive, regulatory or other factors that could have material adverse effects on our future results. Past financial performance may not be a reliable indicator of future performance, and historical trends should not be used to anticipate results or trends in future periods. If any of these risks actually occurs, our business, financial condition, results of operations or cash flow could be seriously harmed. This could cause the trading price of our common stock to decline, resulting in a loss of all or part of your investment. Please also read carefully the section below entitled "Forward-Looking Statements."

FORWARD-LOOKING STATEMENTS

This prospectus and the documents we have filed with the SEC that are incorporated by reference contain "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act. These statements relate to future events or to our future operating or financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performances or achievements expressed or implied by the forward-looking statements. All statements other than statements of historical facts contained in this prospectus, including statements regarding our future results of operations and financial condition, business strategy and plans and objectives of management for future operations, are forward-looking statements. In some cases, forward-looking statements may be identified by words such as "anticipate," "believe," "continue," "could," "design," "estimate," "expect," "intend," "may," "plan," "potentially," "predict," "project," "should," "will" or the negative of these terms or other similar expressions.

We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our financial condition, results of operations, business strategy and financial needs. These forward-looking statements are subject to a number of known and unknown risks, uncertainties and assumptions, including risks described in the section titled "Risk Factors" and elsewhere in this prospectus and in our most recent [Annual Report on Form 10-K](#) and [Quarterly Report on Form 10-Q](#), as well as any amendments thereto reflected in subsequent filings with the SEC, which are incorporated by reference into this prospectus in their entirety, together with other information in this prospectus, the documents incorporated by reference and any free writing prospectus that we may authorize for use in connection with a specific offering. These factors include, among other things:

- the success, cost and timing of our product development activities and clinical trials;
- our expectations about the timing of achieving regulatory approval and the cost of our development programs;
- our ability to obtain funding for our operations, including funding necessary to complete further development and commercialization of our product candidates;

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- the commercialization of our product candidates, if approved;
- our plans to research, develop and commercialize our product candidates;
- our ability to maintain, expand, protect and enforce our intellectual property portfolio;
- our ability to operate our business without infringing, misappropriating or otherwise violating the intellectual property rights of third parties;
- our ability to attract collaborators with development, regulatory and commercialization expertise;
- our expectations regarding our ability to obtain and maintain intellectual property protection for our product candidate;
- our ability to reach agreements and work with third parties in connection with the development and commercialization of our product candidates;
- the size and growth potential of the markets for our product candidates, and our ability to serve those markets;
- the rate and degree of market acceptance of our product candidates;
- regulatory developments in the United States and foreign countries;
- our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately;
- the success of competing therapies that are or may become available;
- our ability to attract and retain key scientific or management personnel;
- the accuracy of our estimates regarding expenses, future revenue, capital requirements and needs for additional financing;
- our expectations regarding the period during which we qualify as an emerging growth company under the JOBS Act; and
- our ability to maintain proper and effective internal controls.

These risks are not exhaustive. Other sections of this prospectus may include additional factors that could harm our business and financial performance. Moreover, we operate in a very competitive and rapidly changing environment. New risk factors emerge from time to time, and it is not possible for our management to predict all risk factors nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ from those contained in, or implied by, any forward-looking statements.

You should not rely upon forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance or achievements. Except as required by law, we undertake no obligation to update publicly any forward-looking statements for any reason after the date of this prospectus or to conform these statements to actual results or to changes in our expectations.

In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this prospectus, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all relevant information. These statements are inherently uncertain and investors are cautioned not to unduly rely upon these statements.

You should read this prospectus and the documents that we reference in this prospectus and have filed as exhibits to the registration statement of which this prospectus is a part with the understanding that our actual future results, levels of activity, performance and achievements may be different from what we expect. We qualify all of our forward-looking statements by these cautionary statements.

USE OF PROCEEDS

Except as described in any applicable prospectus supplement or in any free writing prospectuses we have authorized for use in connection with a specific offering, we currently intend to use the net proceeds from this offering for working capital and general corporate purposes, which may include, among other things, funding research and development, clinical trials, vendor payables, potential regulatory submissions, hiring additional personnel and capital expenditures.

DESCRIPTION OF CAPITAL STOCK

As of the date of this prospectus, our certificate of incorporation, authorizes us to issue up to 90,000,000 shares of common stock, \$0.00001 par value per share, and 10,000,000 shares of preferred stock, \$0.00001 par value per share. As of September 30, 2019, 27,206,447 shares of common stock were outstanding and no shares of preferred stock were outstanding.

The following summary describes the material terms of our capital stock. The description of capital stock is qualified by reference to our certificate of incorporation and our bylaws.

Common Stock

Voting Rights

Holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of stockholders, including the election of directors, and do not have cumulative voting rights. Accordingly, the holders of a majority of the outstanding shares of common stock entitled to vote in any election of directors can elect all of the directors standing for election, if they so choose, other than any directors that holders of any preferred stock we may issue may be entitled to elect.

Dividend Rights

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

Liquidation

In the event of our liquidation, dissolution or winding up, the holders of common stock will be entitled to share ratably in the assets legally available for distribution to stockholders after the payment of or provision for all of our debts and other liabilities, subject to the prior rights of any preferred stock then outstanding.

Rights and Preferences

Holders of common stock have no preemptive or conversion rights or other subscription rights and there are no redemption or sinking funds provisions applicable to the common stock. The rights, preferences and privileges of 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 and issue in the future.

Preferred Stock

Our board of directors may, without further action by our stockholders, fix the rights, preferences, privileges and restrictions of up to an aggregate of 10,000,000 shares of preferred stock in one or more series and authorize their issuance. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting any series or the designation of such series, any or all of which may be greater than the rights of our common stock. The issuance of our preferred stock could adversely affect the voting power of holders of our common stock and the likelihood that such holders will receive dividend payments and payments upon liquidation. In addition, the issuance of preferred stock could have the effect of delaying, deferring or preventing a change of control or other corporate action.

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The following summary of terms of our preferred stock is not complete. You should refer to the provisions of our certificate of incorporation and bylaws and the resolutions containing the terms of each class or series of the preferred stock which have been or will be filed with the SEC at or prior to the time of issuance of such class or series of preferred stock and described in the applicable prospectus supplement. The applicable prospectus supplement may also state that any of the terms set forth herein are inapplicable to such series of preferred stock, provided that the information set forth in such prospectus supplement does not constitute material changes to the information herein such that it alters the nature of the offering or the securities offered.

We will fix the designations, voting powers, preferences and rights of the preferred stock of each series we issue under this prospectus, as well as the qualifications, limitations or restrictions thereof, in the 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. We will describe in the applicable prospectus supplement the terms of the series of preferred stock being offered, including, to the extent applicable:

- 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;
- the provisions for a sinking fund;
- 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 of the preferred stock;
- preemptive rights;
- restrictions on transfer, sale or other assignment;
- whether interests in the preferred stock will be represented by depositary shares;
- a discussion of material United States 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;

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- 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.

If we issue shares of preferred stock under this prospectus, the shares will be fully paid and non-assessable.

The issuance of preferred stock could adversely affect the voting power of holders of common stock and reduce the likelihood that common stockholders will receive dividend payments and payments upon liquidation. The issuance could have the effect of decreasing the market price of the common stock. The issuance of preferred stock also could have the effect of delaying, deterring or preventing a change in control of us.

Options, Restricted Stock Units and Warrants

As of September 30, 2019, (i) stock options to purchase an aggregate of 2,601,566 shares of common stock and 284,445 restricted stock units were outstanding under our 2016 Equity Incentive Plan, or 2016 Plan, and (ii) an additional 579,220 shares of common stock (plus any shares that might in the future be returned to the 2016 Plan as a result of the repurchase of shares or the cancellation or expiration of awards) remained available for future issuance under the 2016 Plan.

As of September 30, 2019, (i) stock options to purchase an aggregate of 470,000 shares of common stock were outstanding under our 2018 Inducement Plan, or Inducement Plan, and (ii) an additional 280,000 shares of common stock (plus any shares that might in the future be returned to the Inducement Plan as a result of the repurchase of shares or the cancellation or expiration of options) remained available for future issuance under the Inducement Plan.

As of September 30, 2019, stock options to purchase an aggregate of 638,065 shares of common stock were outstanding under our 2007 Stock Option Plan, or 2007 Plan, and no shares remained available for future issuance under the 2007 Plan.

As of September 30, 2019, no shares of common stock were outstanding under our 2016 Employee Stock Purchase Plan, or ESPP, and 577,993 shares remained available for future issuance under the ESPP.

As of September 30, 2019, we had outstanding warrants to purchase an aggregate of 2,750,000 shares of common stock at a weighted average exercise price of \$12.50 per share and outstanding warrants to purchase an aggregate of 400,000 shares of common stock at a weighted average exercise price of \$0.00001 per share.

Anti-Takeover Effects of Delaware Law and our Certificate of Incorporation and Bylaws

Some provisions of Delaware law, our certificate of incorporation and our bylaws contain provisions that could make the following transactions more difficult: an acquisition of us by means of a tender offer; an acquisition of us by means of a proxy contest or otherwise; or the removal of our incumbent officers and directors. It is possible that these provisions could make it more difficult to accomplish or could deter transactions that stockholders may otherwise consider to be in their best interest or in our best interests, including transactions which provide for payment of a premium over the market price for our shares.

These provisions, summarized below, are intended to discourage coercive takeover practices and inadequate takeover bids. These provisions are also designed to encourage persons seeking to acquire control of us to first negotiate with our board of directors. We believe that the benefits of the increased

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protection of our potential ability to negotiate with the proponent of an unfriendly or unsolicited proposal to acquire or restructure us outweigh the disadvantages of discouraging these proposals because negotiation of these proposals could result in an improvement of their terms.

Undesignated Preferred Stock—The ability to authorize undesignated preferred stock makes it possible for our board of directors to issue preferred stock with voting or other rights or preferences that could impede the success of any attempt to change control of us. These and other provisions may have the effect of deterring hostile takeovers or delaying changes in control or management of our company.

Stockholder Meetings—Our bylaws provide that a special meeting of stockholders may be called only by our chairman of the board, chief executive officer or president, or by a resolution adopted by a majority of our board of directors.

Requirements for Advance Notification of Stockholder Nominations and Proposals—Our bylaws establish advance notice procedures with respect to stockholder proposals to be brought before a stockholder meeting and the nomination of candidates for election as directors, other than nominations made by or at the direction of the board of directors or a committee of the board of directors.

Elimination of Stockholder Action by Written Consent—Our certificate of incorporation and bylaws eliminate the right of stockholders to act by written consent without a meeting.

Staggered Board—Our board of directors is divided into three classes. The directors in each class will serve for a three-year term, one class being elected each year by our stockholders. This system of electing and removing directors may tend to discourage a third-party from making a tender offer or otherwise attempting to obtain control of us, because it generally makes it more difficult for stockholders to replace a majority of the directors.

Removal of Directors—Our certificate of incorporation provides that no member of our board of directors may be removed from office by our stockholders except for cause and, in addition to any other vote required by law, upon the approval of not less than two thirds of the total voting power of all of our outstanding voting stock then entitled to vote in the election of directors.

Stockholders Not Entitled to Cumulative Voting—Our certificate of incorporation does not permit stockholders to cumulate their votes in the election of directors. Accordingly, the holders of a majority of the outstanding shares of our common stock entitled to vote in any election of directors can elect all of the directors standing for election, if they choose, other than any directors that holders of our preferred stock may be entitled to elect.

Delaware Anti-Takeover Statute—We are subject to Section 203 of the Delaware General Corporation Law, which prohibits persons deemed to be "interested stockholders" from engaging in a "business combination" with a publicly held Delaware corporation for three years following the date these persons become interested stockholders unless the business combination is, or the transaction in which the person became an interested stockholder was, approved in a prescribed manner or another prescribed exception applies. Generally, an "interested stockholder" is a person who, together with affiliates and associates, owns, or within three years prior to the determination of interested stockholder status did own, 15% or more of a corporation's voting stock. Generally, a "business combination" includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to the interested stockholder. The existence of this provision may have an anti-takeover effect with respect to transactions not approved in advance by the board of directors.

Choice of Forum—Our certificate of incorporation provides that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware is the exclusive forum for the following types of actions or proceedings under Delaware statutory or common law:

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(1) any derivative action or proceeding brought on our behalf; (2) any action asserting a claim of breach of a fiduciary duty or other wrongdoing by any of our directors, officers, employees or agents to us or our stockholders; (3) any action asserting a claim against us arising pursuant to any provision of the General Corporation Law of the State of Delaware or our certificate of incorporation or bylaws; (4) any action to interpret, apply, enforce or determine the validity of our certificate of incorporation or bylaws; or (5) any action asserting a claim governed by the internal affairs doctrine. This provision does not apply to suits brought to enforce a duty or liability created by the Exchange Act or any other claim for which the U.S. federal courts have exclusive jurisdiction. Our certificate of incorporation also provides that any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock will be deemed to have notice of and to have consented to this choice of forum provision. It is possible that a court of law could rule that the choice of forum provision contained in our certificate of incorporation is inapplicable or unenforceable if it is challenged in a proceeding or otherwise.

Amendment of Charter Provisions—The amendment of any of the above provisions, except for the provision making it possible for our board of directors to issue preferred stock, would require approval by holders of at least two thirds of the total voting power of all of our outstanding voting stock.

The provisions of Delaware law, our certificate of incorporation and our bylaws could have the effect of discouraging others from attempting hostile takeovers and, as a consequence, they may also inhibit temporary fluctuations in the market price of our common stock that often result from actual or rumored hostile takeover attempts. These provisions may also have the effect of preventing changes in the composition of our board and management. It is possible that these provisions could make it more difficult to accomplish transactions that stockholders may otherwise deem to be in their best interests.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company, LLC. The transfer agent's address is 6201 15th Avenue, Brooklyn, New York 11219. The transfer agent for any series of preferred stock that we may offer under this prospectus will be named and described in the prospectus supplement for that series.

Listing on the Nasdaq Global Market

Our common stock is listed on the Nasdaq Global Market under the symbol "PTGX." The applicable prospectus supplement will contain information, where applicable, as to any other listing, if any, on the Nasdaq Global Market or any securities market or other exchange of the preferred stock covered by such prospectus supplement.

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 have filed 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 does 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;

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- 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;
- if other than the full principal amount thereof, the portion of the principal amount of debt securities of the series which shall be payable upon declaration of acceleration of the maturity thereof;
- 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;

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- 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;

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- 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, 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.

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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

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

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- reducing the percentage of debt securities, the holders of which are required to consent to any amendment, supplement, modification or waiver.

Discharge

Each indenture provides 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 provides 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

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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 will be governed by and construed in accordance with the internal 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 supplement and free writing prospectus, 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 offered independently or in combination with common stock, preferred stock or debt securities offered by any prospectus supplement. 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 in more detail in the applicable prospectus supplement. The following description of warrants will apply to the warrants offered by this prospectus unless we provide otherwise in the applicable prospectus supplement. The applicable prospectus supplement for a particular series of warrants may specify different or additional terms.

We have filed forms of the warrant agreements and forms of warrant certificates containing the terms of the warrants that may be offered as exhibits to the registration statement of which this prospectus is a part. 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 and/or the warrant agreement and warrant certificate, as applicable, that contain the terms of the particular series of warrants we are offering, and any supplemental agreements, before the issuance of such warrants. The following summaries of material terms and provisions of the warrants are subject to, and qualified in their entirety by reference to, all the provisions of the form of warrant and/or the warrant agreement and warrant certificate, as applicable, and any supplemental agreements applicable to a particular series of warrants that we may offer under this prospectus. We urge you to read the applicable prospectus supplement related to the particular series of warrants that we may offer under this prospectus, as well as any related free writing prospectus, and the complete form of warrant and/or the warrant agreement and warrant certificate, as applicable, and any supplemental agreements, that contain the terms of the warrants.

General

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

- the offering price and aggregate number of warrants offered;
- the currency 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;
- 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, 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 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;
- any provisions for changes to or adjustments in the exercise price or number of securities issuable upon exercise of the warrants;

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- 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 U.S. federal income tax considerations 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. The warrants may be exercised as set forth in the prospectus supplement relating to the warrants offered. Unless we otherwise specify in the applicable prospectus supplement, warrants may be exercised at any time up to the close of business on the expiration date set forth in the prospectus supplement relating to the warrants offered thereby. After the close of business on the expiration date, unexercised warrants will become void.

Upon receipt of payment and the warrant or warrant certificate, as applicable, properly completed and duly executed at the corporate trust office of the warrant agent, if any, or any other office, including ours, indicated in the prospectus supplement, we will, as soon as practicable, issue and deliver the securities purchasable upon such exercise. If less than all of the warrants (or the warrants represented by such warrant certificate) are exercised, a new warrant or a new warrant certificate, as applicable, will be issued for the remaining warrants.

Governing Law

Unless we otherwise specify in the applicable prospectus supplement, the warrants and any 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, if any, 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, depository or warrant agent 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. Securities issued in global form will be registered in the name of the depository or its participants. Consequently, for securities issued in global form, 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

We may terminate a global security or issue securities in non-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 applicable 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 and of any third parties 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 legal 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 the indenture or for other purposes. In such an event, we would seek approval only from the 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 depositary'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 depositary. 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 depositary. Unless we specify otherwise in the applicable prospectus supplement, DTC will be the depositary 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 depositary, its nominee or a successor depositary, 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 depositary, 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 depositary or with

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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 in global form only, 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

The rights of an indirect holder 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 in the form of a global security, 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, broker or other financial institution 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 a 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 depository's policies, which may change from time to time, will govern payments, transfers, exchanges and other matters relating to an investor's interest in a global security;
- we and any applicable trustee have no responsibility for any aspect of the depository's actions or for its records of ownership interests in a global security, nor do we or any applicable trustee supervise the depository in any way;
- the depository may, and we understand that DTC will, require that those who purchase and sell interests in a global security within its book-entry system use immediately available funds, and your bank, broker or other financial institution may require you to do so as well; and
- financial institutions that participate in the depository's book-entry system, and through which an investor holds its interest in a 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, the global security will terminate and interests in it will be exchanged for physical certificates representing those interests. After that exchange, the choice of

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whether to hold securities directly or in street name will be up to the investor. Investors must consult their own banks, brokers or other financial institutions to find out how to have their interests in securities transferred to their own name, 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, the 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 not we or 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 our securities covered by this prospectus in any of three ways (or in any combination):

- to or through underwriters or dealers;
- directly to one or more purchasers; or
- through agents.

We may distribute the securities:

- from time to time in one or more transactions at a fixed price or prices, which may be changed from time to time;
- at market prices prevailing at the time of sale;
- at prices related to the prevailing market prices; or
- at negotiated prices.

Each time we offer and sell securities covered by this prospectus, we will provide a prospectus supplement or supplements that will describe the method of distribution and set forth the terms of the offering, including:

- the name or names of any underwriters, dealers or agents;
- the amounts of securities underwritten or purchased by each of them;
- the purchase price of securities and the proceeds we will receive from the sale;
- any over-allotment options under which underwriters may purchase additional securities from us;
- any underwriting discounts or commissions or agency fees and other items constituting underwriters' or agents' compensation;
- the public offering price of the securities;
- any discounts, commissions or concessions allowed or reallocated or paid to dealers; and
- any securities exchange or market on which the securities may be listed.

Any public offering price and any discounts or concessions allowed or reallocated or paid to dealers may be changed from time to time. We may determine the price or other terms of the securities offered under this prospectus by use of an electronic auction. We will describe how any auction will determine the price or any other terms, how potential investors may participate in the auction and the nature of the obligations of the underwriter, dealer or agent in the applicable prospectus supplement.

Underwriters or dealers may offer and sell the offered securities from time to time in one or more transactions, including negotiated transactions, at a fixed public offering price or at varying prices determined at the time of sale. If underwriters or dealers are used in the sale of any securities, the securities will be acquired by the underwriters or dealers for their own account and may be resold from time to time in one or more transactions described above. The securities may be either offered to the public through underwriting syndicates represented by managing underwriters, or directly by underwriters or dealers. Generally, the underwriters' or dealers' obligations to purchase the securities will be subject to certain conditions precedent. The underwriters or dealers will be obligated to purchase all of the securities if they purchase any of the securities, unless otherwise specified in the prospectus supplement. We may use underwriters with whom we have a material relationship. We will describe the nature of any such relationship in the prospectus supplement, naming the underwriter.

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We may sell the securities through agents from time to time. The prospectus supplement will name any agent involved in the offer or sale of the securities and any commissions we pay to them. Generally, any agent will be acting on a best efforts basis for the period of its appointment. We may authorize underwriters, dealers or agents to solicit offers by certain purchasers to purchase the 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. The contracts will be subject only to those conditions set forth in the prospectus supplement, and the prospectus supplement will set forth any commissions we pay for solicitation of these contracts.

Agents, dealers and underwriters may be entitled to indemnification by us against certain civil liabilities, including liabilities under the Securities Act, or to contribution with respect to payments which the agents, dealers or underwriters may be required to make in respect thereof. Agents, dealers and underwriters may be customers of, 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 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.

Any underwriter may engage in over-allotment, stabilizing transactions, short covering transactions and penalty bids in accordance with Regulation M under the Securities Exchange Act of 1934, as amended. Over-allotment involves sales in excess of the offering size, which create a short position. This short sales position may involve either "covered" short sales or "naked" short sales. Covered short sales are short sales made in an amount not greater than the underwriters' over-allotment option to purchase additional securities in this offering described above. The underwriters may close out any covered short position either by exercising their over-allotment option or by purchasing securities in the open market. To determine how they will close the covered short position, the underwriters will consider, among other things, the price of securities available for purchase in the open market, as compared to the price at which they may purchase securities through the over-allotment option. Naked short sales are short sales in excess of the over-allotment option. The underwriters must close out any naked short position by purchasing securities in the open market. A naked short position is more likely to be created if the underwriters are concerned that, in the open market after pricing, there may be downward pressure on the price of the securities that could adversely affect investors who purchase securities in this offering. Stabilizing transactions permit bids to purchase the underlying security for the purpose of fixing the price of the security so long as the stabilizing bids do not exceed a specified maximum. 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 covering transaction to cover short positions.

Any underwriters who are qualified market makers on the Nasdaq Global Market may engage in passive market making transactions in our common stock, preferred stock, warrants and debt securities, as applicable, 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.

In compliance with guidelines of the Financial Industry Regulatory Authority, or FINRA, the maximum consideration or discount 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.

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Similar to other purchase transactions, an underwriter's purchase to cover the syndicate short sales or to stabilize the market price of our securities may have the effect of raising or maintaining the market price of our securities or preventing or mitigating a decline in the market price of our securities. As a result, the price of our securities may be higher than the price that might otherwise exist in the open market. The imposition of a penalty bid might also have an effect on the price of the securities if it discourages resales of the securities.

Neither we nor the underwriters make any representation or prediction as to the effect that the transactions described above may have on the price of the securities. If such transactions are commenced, they may be discontinued without notice at any time.

LEGAL MATTERS

Unless otherwise indicated in the applicable prospectus supplement, the validity of the securities offered by this prospectus, and any supplement thereto, will be passed upon for us by Cooley LLP.

EXPERTS

The financial statements incorporated in this Prospectus by reference to the [Annual Report on Form 10-K for the year ended December 31, 2018](#) have been so incorporated in reliance on the report of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND MORE INFORMATION

This prospectus is part of a registration statement we filed with the SEC. This prospectus does not contain all of the information set forth in the registration statement and the exhibits to the registration statement. For further information with respect to us and the securities 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 securities offered by this prospectus.

We file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public at the SEC's website at <http://www.sec.gov>.

INCORPORATION OF CERTAIN INFORMATION BY REFERENCE

The SEC allows us to "incorporate by reference" the information we file with it, which means that we can disclose important information to you by referring you to those documents instead of having to repeat the information in this prospectus. The information incorporated by reference is considered to be part of this prospectus, and later information that we file with the SEC will automatically update and supersede this information. We incorporate by reference the documents listed below and any future filings (including those made after the date of the initial filing of the registration statement of which this prospectus is a part and prior to the effectiveness of such registration statement) we will make with the SEC under Sections 13(a), 13(c), 14, or 15(d) of the Exchange Act until the termination of the offering of the shares covered by this prospectus (other than information furnished under Item 2.02 or Item 7.01 of Form 8-K):

- our [annual report on Form 10-K for the year ended December 31, 2018, filed with the SEC on March 12, 2019](#), including the information specifically incorporated by reference therein from our [definitive proxy statement on Schedule 14A, filed on April 26, 2019](#);
- [our Quarterly Report on Form 10-Q for the quarter ended March 31, 2019, filed with the SEC on May 8, 2019](#);
- [our Quarterly Report on Form 10-Q for the quarter ended June 30, 2019, filed with the SEC on August 7, 2019](#);
- [our Quarterly Report on Form 10-Q for the quarter ended September 30, 2019, filed with the SEC on November 6, 2019](#);
- our current reports on Form 8-K, filed with the SEC on [March 25, 2019](#), [May 8, 2019 \(Item 1.01\)](#), [May 13, 2019](#), [May 29, 2019](#), [June 13, 2019](#) and [October 31, 2019](#); and
- [the description of our common stock set forth in our registration statement on Form 8-A, filed with the SEC on August 9, 2016, including any amendments thereto or reports filed for the purposes of updating this description](#).

You can request a copy of these filings, at no cost, by writing or telephoning us at the following address or telephone number:

Protagonist Therapeutics, Inc.
7707 Gateway Boulevard, Suite 140
Newark, California 94560
(510) 474-0170
Attn: Chief Financial Officer



Up To \$75,000,000 of Shares

Common Stock

PROSPECTUS SUPPLEMENT

Jefferies

November 27, 2019
