

This preliminary prospectus supplement relates to an effective registration statement under the Securities Act of 1933, as amended, but is not complete and may be changed. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell these securities, and we are not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to completion, dated December 10, 2020

Filed Pursuant to Rule 424(b)(5)
Registration No. 333-251254

**Preliminary prospectus supplement
(To prospectus dated December 10, 2020)**

\$100,000,000



Common stock

We are offering \$100,000,000 of shares of our common stock. Our common stock is listed on the Nasdaq Global Market under the symbol "PTGX." On December 9, 2020, the last reported sale price of our common stock was \$23.44 per share.

We are an "emerging growth company" under applicable Securities and Exchange Commission rules and are eligible for reduced public company disclosure requirements.

Our business and an investment in our common stock involve significant risks. These risks are described under the caption "Risk Factors" beginning on page S-9 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 passed upon the accuracy or adequacy of this prospectus supplement or the accompanying prospectus. Any representation to the contrary is a criminal offense.

	Per share	Total
Public offering price	\$	\$
Underwriting discounts and commissions ⁽¹⁾	\$	\$
Proceeds, before expenses, to Protagonist Therapeutics, Inc.	\$	\$

(1) See "Underwriting" for additional disclosure regarding underwriting compensation.

The underwriters may also purchase up to an additional \$15,000,000 of shares of our common stock from us at the public offering price, less the underwriting discount, within 30 days from the date of this prospectus supplement. See "Underwriting" for more information.

The underwriters expect to deliver the shares to purchasers against payment on or about December 10, 2020 through the book-entry facilities of The Depository Trust Company.

Joint Book-running Managers

J.P. MorganSVB LeerinkPiper SandlerBMO Capital Markets

Table of contents**Prospectus supplement**

	Page
ABOUT THIS PROSPECTUS SUPPLEMENT	S-2
PROSPECTUS SUPPLEMENT SUMMARY	S-3
RISK FACTORS	S-9
FORWARD-LOOKING STATEMENTS	S-12
USE OF PROCEEDS	S-13
CAPITALIZATION	S-14
DILUTION	S-16
MATERIAL U.S. FEDERAL INCOME TAX CONSEQUENCES TO NON-U.S. HOLDERS	S-18
UNDERWRITING	S-22
LEGAL MATTERS	S-29
EXPERTS	S-29
WHERE YOU CAN FIND MORE INFORMATION	S-29
INCORPORATION OF CERTAIN INFORMATION BY REFERENCE	S-29

Prospectus

	Page
ABOUT THIS PROSPECTUS	ii
PROSPECTUS SUMMARY	1
THE SECURITIES WE MAY OFFER	5
RISK FACTORS	8
FORWARD-LOOKING STATEMENTS	9
USE OF PROCEEDS	11
DESCRIPTION OF CAPITAL STOCK	12
DESCRIPTION OF DEBT SECURITIES	17
DESCRIPTION OF WARRANTS	24
LEGAL OWNERSHIP OF SECURITIES	26
PLAN OF DISTRIBUTION	29
LEGAL MATTERS	31
EXPERTS	31
WHERE YOU CAN FIND MORE INFORMATION	31
INCORPORATION OF CERTAIN INFORMATION BY REFERENCE	31

About this prospectus supplement

This document is in two parts. The first part is this prospectus supplement, which describes the specific 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 herein. The second part, the accompanying prospectus, 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 and the information contained in the accompanying prospectus or any document incorporated by reference therein filed prior to the date of this prospectus supplement, you should rely on the information in this prospectus supplement; provided that 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 in 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 the underwriters have not, authorized anyone to provide any information other than that contained 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 the underwriters take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. This prospectus supplement and the accompanying prospectus do not constitute an offer to sell, or a solicitation of an offer to purchase, the securities offered by this prospectus supplement and the accompanying prospectus in any jurisdiction to or from any person to whom or from whom it is unlawful to make such offer or solicitation of an offer in such jurisdiction. The information contained in this prospectus supplement, the accompanying prospectus, any free writing prospectus that we have authorized for use in connection with this offering, including the documents incorporated by reference herein or therein is accurate only as of the respective dates thereof, regardless of the time of delivery of this prospectus supplement and the accompanying prospectus or of any sale of our common stock. It is important for you to read and consider all information contained in this prospectus supplement, the accompanying prospectus and any free writing prospectus that we have authorized for use in connection with this offering, including the documents incorporated by reference herein and therein, in making your investment decision. You should also read and consider the information in the documents to which we have referred you in the sections entitled “Where You Can Find More Information” and “Incorporation of Certain Information by Reference” in this prospectus supplement and in the accompanying prospectus.

We and the underwriters 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 the 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 the 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 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 referenced herein or 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.

Prospectus supplement summary

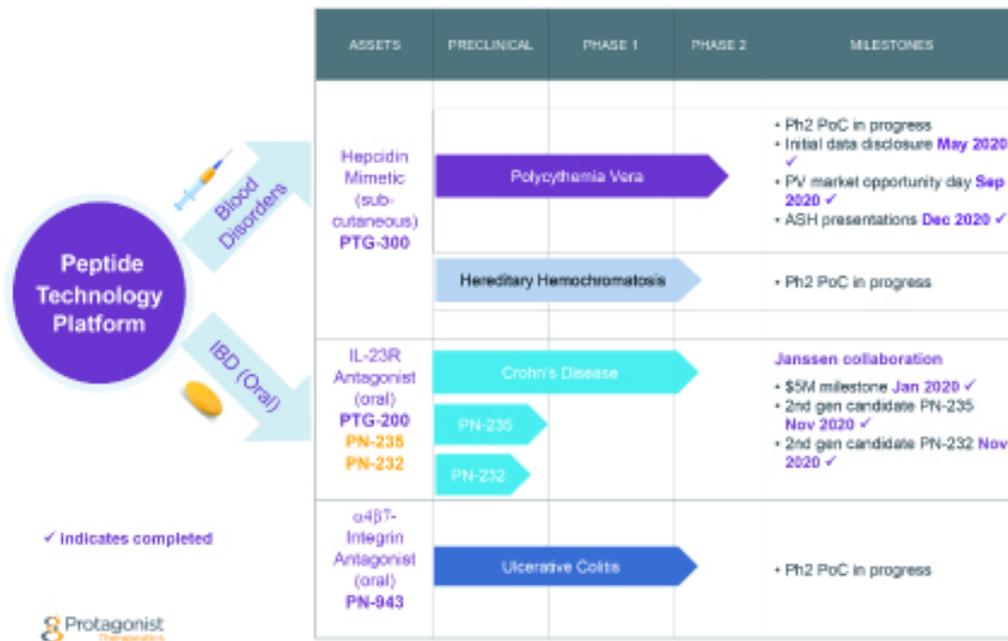
This summary highlights selected information contained elsewhere in this prospectus supplement or incorporated by reference herein and does not contain all of the information that you need to consider in making your investment decision. You should carefully read the entire prospectus supplement, the accompanying prospectus or any free writing prospectus that we have authorized for use in connection with this offering, including the risks of investing in our securities discussed under the heading “Risk Factors” contained in this prospectus supplement, the accompanying prospectus or any free writing prospectus that we have authorized for use in connection with this offering, 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 that utilizes a proprietary technology platform to discover and develop novel peptide-based drugs to address significant unmet medical needs and transform existing treatment paradigms for patients. We have three assets in various stages of clinical development derived from this platform.

Our product pipeline



Our most advanced clinical asset, PTG-300, is an injectable hepcidin mimetic in development for the potential treatment of erythrocytosis, iron overload and other blood disorders. Hepcidin is a key hormone in regulating iron equilibrium and is critical to the proper development of red blood cells. PTG-300 mimics the effect of the natural hormone hepcidin, but with greater potency, solubility and stability. We initiated a Phase 2 proof of concept (“PoC”) study in polycythemia vera (“PV”) in the third quarter of 2019 and a Phase 2 PoC study in hereditary hemochromatosis (“HH”) in January 2020. We believe the interim results from our initial Phase 2 PV efficacy data from a small number of patients provide evidence regarding the potential of PTG-300 to eliminate the

need for phlebotomy by controlling hematocrit levels below 45% on an individual patient basis. The American Society for Hematology accepted four posters and one oral presentation relating to PTG-300 for its virtual annual meeting held in December 2020, including updated Phase 2 results for PTG-300 in PV. PTG-300 has a unique mechanism of action in the potential treatment of PV, which may enable it to decrease and maintain hematocrit levels within the range of recommended clinical guidelines without causing the iron deficiency that may occur with frequent phlebotomy. We have announced the selection of PV as our first indication for a potential pivotal study to begin in 2021. In June 2020, the U.S. Food and Drug Administration granted orphan drug designation for PTG-300 for the treatment of PV. In October 2020, the European Medicines Agency granted orphan drug designation for PTG-300 for the treatment of PV. In December 2020, the FDA granted Fast Track designation for PTG-300 for the treatment of PV. We discontinued development of PTG-300 for anemia associated with beta-thalassemia and myelodysplastic syndromes during the first quarter of 2020 and are redirecting the majority of our PTG-300 efforts to the PV indication, while also continuing our exploration of PTG-300 in HH.

Our clinical assets PTG-200 and PN-943 are orally delivered investigational 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 are designed to block biological pathways currently targeted by marketed injectable antibody drugs. Our orally stable peptide approach may offer 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 oral therapy. As a result, if successfully developed and approved, we believe they may transform the existing treatment paradigm for IBD.

PTG-200 (also referenced as JNJ-67864238) is an investigational, orally delivered gut-restricted Interleukin-23 receptor (“IL-23R”) antagonist for the treatment of IBD. In May 2017, we 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 certain related compounds for all indications, including IBD. The agreement with Janssen was amended in May 2019 to expand the collaboration by supporting efforts towards second-generation IL-23R antagonists, triggering a \$25.0 million milestone payment to us. In January 2020, as part of the expanded research collaboration, we announced the identification and nomination of an orally delivered IL-23R antagonist peptide as a second-generation development candidate, triggering a \$5.0 million milestone payment to us. Janssen initiated a global Phase 2 PoC clinical study for PTG-200 in moderate-to-severe CD in the fourth quarter of 2019. Because of the COVID-19 pandemic, we have suspended guidance on a timeline for PTG-200 Phase 2 study completion. In October 2020, we announced the selection of two second-generation IL-R antagonists for advancement into clinical development, PN-235 (also referenced as JNJ-77242113) and PN-232 (also referenced as JNJ-75105186). The advancement of three different oral co-development candidates provides us with several strategic options for development in multiple indications. We are also continuing our joint research efforts to identify additional IL-23R antagonists.

PN-943 is an investigational, orally delivered, gut-restricted, alpha-4-beta-7 (“ $\alpha 4\beta 7$ ”) specific integrin antagonist. We developed PN-943 as a potentially more potent orally delivered, gut-restricted $\alpha 4\beta 7$ backup compound to PTG-100, our first-generation orally delivered gut-restricted $\alpha 4\beta 7$ inhibitor that was being developed for treatment of IBD. In 2019, we completed a Phase 1 single ascending dose and multiple ascending dose clinical study of PN-943 in healthy volunteers to evaluate safety, pharmacokinetics and pharmacodynamics. The pharmacodynamic results indicated that the administration of PN-943 was well tolerated and showed of target engagement that were suggestive of higher potency for PN-943 as compared to PTG-100. We submitted a U.S. Investigational New Drug application with the U.S. Food and Drug Administration (the “FDA”) for PN-943 in December 2019, which took effect in January 2020, and have initiated a Phase 2 PoC study in UC. In light of the COVID-19 pandemic, we are continuing to review all aspects of the planned Phase 2 study and are suspending guidance on a timeline for study progress and completion.

Our clinical assets are all derived from our proprietary discovery platform. Our platform enables us to engineer novel, structurally constrained peptides that are designed to retain key advantages of both orally delivered small molecules and injectable antibody drugs, in an effort to overcome many of their limitations as therapeutic

agents. Importantly, constrained peptides can be designed to potentially 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 potential 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 (the “First Amendment”). 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 First Amendment. During the fourth quarter of 2019, we became eligible to receive a cash payment of \$5.0 million upon the successful nomination of a second-generation development candidate, which we received during the first quarter of 2020.

Impact of COVID-19 on our business

We are subject to risks and uncertainties as a result of the COVID-19 pandemic. We are continuing to closely monitor the impact of the COVID-19 pandemic on our business and have taken and continue to take proactive efforts to protect the health and safety of our patients, clinical research staff and employees, and to maintain business continuity. The extent of the impact of the COVID-19 pandemic on our activities is highly uncertain and difficult to predict, as the pandemic and the response to the pandemic continue to rapidly evolve. Capital markets and economies worldwide have also been negatively impacted by the COVID-19 pandemic, and the pandemic has contributed to a global economic recession. Such economic disruption could have a material adverse effect on our business. Policymakers around the globe have responded with fiscal policy actions to support the healthcare industry and economy as a whole. The magnitude and overall effectiveness of these actions remains uncertain.

The severity of the impact of the COVID-19 pandemic on our activities will depend on a number of factors, including, but not limited to, the duration and severity of the pandemic, including the severity of any additional periods of increases or spikes in the number of cases in the areas we and our suppliers operate and areas where our clinical trial sites are located. Accordingly, the extent and severity of the impact on our existing and planned clinical trials and collaboration activities, all of which are uncertain and cannot be predicted. We have experienced delays in our existing and planned clinical trials due to the worldwide impacts of the pandemic. Our future results of operations and liquidity could be adversely impacted by further delays in existing and planned clinical trials and collaboration activities, difficulty in recruiting patients for these clinical trials, supply chain disruptions, the ongoing impact on operating activities and employees and the ongoing impact of any initiatives or programs that we may undertake to address financial and operational challenges. The extent to which the COVID-19 pandemic may materially impact our future financial condition, liquidity or results of operations is uncertain.

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, and 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 are the property of their respective owners. We do not intend our use or display of other companies' trademarks, service marks or trade names 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.

Risks associated with our business

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

The offering

Common stock offered by us	\$100,000,000 of shares of common stock, plus up to an additional \$15,000,000 of shares of common stock if the underwriters exercise their option to purchase additional shares in full.
Common stock to be outstanding after this offering	_____ shares, or _____ shares if the underwriters exercise their option to purchase additional shares in full.
Option to purchase additional shares	The underwriters have an option to purchase up to an additional \$15,000,000 of shares of common stock from us. The underwriters can exercise this option at any time within 30 days from the date of this prospectus supplement.
Use of proceeds	We currently intend to use the net proceeds from this offering to fund research and development of our clinical-stage pipeline product candidates, including the continued development of PTG-300, PTG-200 and PN-943, for discovery, research and technology platform optimization and applications, and for working capital and general corporate purposes. Pending these uses, we intend to invest the net proceeds in interest-bearing, investment-grade securities. See “Use of Proceeds” on page S- 13 of this prospectus supplement.
Risk factors	Investing in our common stock involves significant risks. You should read the “Risk Factors” section of this prospectus supplement beginning on page S- 9 and on page 8 of the accompanying prospectus and under similar headings in other documents that are incorporated by reference into this prospectus supplement for a discussion of factors to consider carefully before deciding to invest in shares of our common stock.
The Nasdaq Global Market symbol	Our shares are listed on the Nasdaq Global Market under the symbol “PTGX.”

The number of shares of our common stock to be outstanding after this offering is based on 37,314,873 shares of our common stock outstanding as of September 30, 2020 and excludes:

- 3,480,141 shares of common stock issuable upon the exercise of stock options issued and outstanding under our 2016 Equity Incentive Plan (the “2016 Plan”), as of September 30, 2020, having a weighted average exercise price of \$12.63 per share;
- 262,608 shares of common stock issuable upon the vesting of outstanding restricted stock units, under the 2016 Plan, as of September 30, 2020;
- an aggregate of 552,511 shares of common stock, subject to increase on an annual basis, reserved for future issuance under the 2016 Plan, as of September 30, 2020;
- 603,500 shares of common stock issuable upon the exercise of stock options issued and outstanding under our Amended and Restated 2018 Inducement Plan, as amended (the “Inducement Plan”), as of September 30, 2020, having a weighted average exercise price of \$11.64 per share;

- an aggregate of 630,000 shares of common stock reserved for future issuance under the Inducement Plan, as of September 30, 2020;
- 513,178 shares of common stock issuable upon the exercise of stock options issued and outstanding under our 2007 Equity Incentive Plan, as of September 30, 2020, having a weighted average exercise price of \$3.43 per share;
- 757,647 shares of our common stock reserved for future issuance under our 2016 Employee Stock Purchase Plan, as of September 30, 2020;
- 2,750,000 shares of common stock issuable upon the exercise of warrants outstanding as of September 30, 2020, 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, 2020, at a weighted average exercise price of \$0.00001 per share.
- Subsequent to September 30, 2020, and through the date of this prospectus supplement, we issued and sold an aggregate of 917,879 shares of common stock at an average price of \$21.03 per share pursuant to our at-the-market offering program. The number of shares of common stock to be outstanding immediately following this offering as described herein does not include such shares sold pursuant to our at-the-market offering program.

Unless otherwise indicated, all information in this prospectus supplement assumes no exercise of outstanding options or warrants after September 30, 2020 and no exercise by the underwriters of their option to purchase additional shares of our common stock.

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 for the year ended December 31, 2019](#) and [Quarterly Report on Form 10-Q for the three-month period ended September 30, 2020](#), which are incorporated by reference into this prospectus supplement and the accompanying prospectus in their entirety, 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.”

Risks related to the COVID-19 pandemic

The COVID-19 pandemic could adversely impact our business including our ongoing and planned clinical trials and preclinical and discovery research.

In December 2019, COVID-19 was reported to have surfaced in Wuhan, China. Since then, the virus has spread to numerous other countries, including the United States, resulting in the World Health Organization characterizing COVID-19 as a pandemic. The extent to which the COVID-19 pandemic impacts our business will continue to depend on future developments, which are highly uncertain and cannot be predicted, such as the ultimate geographic spread of the disease, the duration of the outbreak, the development of a vaccine or other treatments, travel restrictions and social distancing in the United States and other countries, business closures or business disruptions and the effectiveness of actions taken in the United States and other countries to contain, ameliorate the impact of and treat the disease and to address its impact, including on financial markets or otherwise. Countries and territories, including the United States, are in varying stages of restrictions and re-openings to address the COVID-19 pandemic. Certain jurisdictions have begun re-opening only to return to restrictions in the face of increases in new COVID-19 cases. As the COVID-19 pandemic continues, we could experience disruptions that could severely impact our business, current and planned clinical trials and preclinical and discovery research, including:

- delays or difficulties in enrolling patients in our ongoing clinical trials and our future clinical trials;
- delays or difficulties in clinical site initiation, including difficulties in recruiting clinical site investigators and clinical site staff;
- diversion of healthcare resources away from the conduct of clinical trials, including the diversion of hospitals serving as our clinical trial sites and hospital staff supporting the conduct of clinical trials;
- interruption of key clinical trial activities, such as clinical trial site monitoring, due to limitations on travel imposed or recommended by federal or state governments, employers and others or interruption of clinical trial subject visits and study procedures, which may impact the integrity of subject data and clinical study endpoints;
- limitations in resources, including our employees, that would otherwise be focused on the conduct of our business or our current or planned clinical trials or preclinical research, including because of sickness, the desire to avoid contact with large groups of people or restrictions on movement or access to our facility as a result of government-imposed “shelter in place” or similar working restrictions;

- interruptions or delays in the operations of the FDA or other regulatory authorities, which may impact review and approval timelines;
- delays in receiving the supplies, materials and services needed to conduct clinical trials and preclinical research;
- changes in regulations as part of a response to the COVID-19 pandemic which may require us to change the ways in which our clinical trials are conducted, which may result in unexpected costs or require us to discontinue the clinical trial altogether;
- interruptions or delays to our development pipeline; and
- delays in necessary interactions with regulators, ethics committees and other important agencies and contractors due to limitations in employee resources or furlough of government or contractor personnel.

In addition, in March 2020, the health officers of six San Francisco Bay Area counties, including Alameda County where our headquarters are located, issued a “shelter-in-place” order, effective March 17, 2020, and on March 19, 2020, the Governor of California, the State Public Health Officer and Director of the California Department of Public Health, ordered all individuals in the State of California to stay home or at their place of residence except as needed to maintain continuity of operations of the federal critical infrastructure sectors. Following updated guidance issued by federal, state and local authorities, our laboratory facilities remain open for research activities that cannot be conducted remotely, with heightened safety measures designed to minimize occupational exposure and reduce transmission of COVID-19 within our workplace. As a result of such county and California state orders and subsequent updated guidance, our non-laboratory employees telecommute at least part-time, which may impact certain of our operations over the near term and long term. Although our laboratory facilities remain open on this basis under these heightened safety measures, we may be forced to, or determine that we should, resume a more restrictive remote work model, whether as a result of spikes or surges in COVID-19 infection, positivity or hospitalization rates or otherwise. These and similar, and perhaps more severe, disruptions in our operations could negatively impact our business, operating results and financial condition.

Further, as a result of the COVID-19 pandemic, the extent and length of which is uncertain, we may be required to develop and implement additional clinical study policies and procedures designed to help protect study participants from the COVID-19 virus, which may include using telemedicine visits, remote monitoring of patients and clinical sites, and measures to ensure that data from clinical studies that may be disrupted as result of the pandemic are collected pursuant to the study protocol and consistent with good clinical practices, with any material protocol deviation reviewed and approved by the site Institutional Review Board. Patients who may miss scheduled appointments, any interruption in study drug supply, or other consequence that may result in incomplete data being generated during a study as a result of the pandemic must be adequately documented and justified. For example, on March 18, 2020, the FDA issued a guidance on conducting clinical trials during the pandemic, which describe a number of considerations for sponsors of clinical trials impacted by the pandemic, including the requirement to include in the clinical study report (or as a separate document) contingency measures implemented to manage the study, and any disruption of the study as a result of the COVID-19 pandemic; a list of all study participants affected by the COVID-19-pandemic related study disruption by unique subject identifier and by investigational site, and a description of how the individual’s participation was altered; and analyses and corresponding discussions that address the impact of implemented contingency measures (e.g., participant discontinuation from investigational product and/or study, alternative procedures used to collect critical safety and/or efficacy data) on the safety and efficacy results reported for the study.

While the extent of the impact of the COVID-19 pandemic on our business and financial results is uncertain, a continued and prolonged public health crisis such as the COVID-19 pandemic could have a material negative impact on our business, financial condition, and operating results.

Additional risks related to this offering

Management will have broad discretion as to the use of the net 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 use 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 4,266,211 shares of our common stock are sold at a price of \$23.44 per share (the last reported sale price of our common stock on the Nasdaq Global Market on December 9, 2020) for aggregate gross proceeds of \$100.0 million, and after deducting commissions and estimated offering expenses payable by us, you would experience immediate dilution of \$17.12 per share, representing the difference between our as adjusted net tangible book value per share as of September 30, 2020 after giving effect to this offering and the public offering price. The exercise of outstanding stock options and warrants 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 contain forward-looking statements, 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 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, and our ability to maintain and operate our business, including our clinical supply chain and ability to initiate and complete preclinical studies and clinical trials, in light of the ongoing COVID-19 pandemic, 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 in our Quarterly Reports on Form 10-Q, as well as any amendments thereto, filed with the Securities and Exchange Commission (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 and in our [Annual Report on Form 10-K for the year ended December 31, 2019](#) and [Quarterly Report on Form 10-Q for the three- and nine-month periods ended September 30, 2020](#), 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 supplement, 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 estimate that the net proceeds to us from our issuance and sale of \$100.0 million of shares of common stock in this offering will be approximately \$93.4 million, or approximately \$107.5 million if the underwriters exercise their option to purchase additional shares in full, in each case after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

We currently intend to use the net proceeds from this offering, together with our cash, cash equivalents and investments, as follows:

- to fund research and development of our clinical-stage pipeline product candidates, including the continued development of PTG-300, PTG-200 and PN-943;
- for discovery, research and technology platform optimization and applications; and
- for working capital and general corporate purposes.

The expected use of the net proceeds from this offering represents our intentions based upon our current plans and business conditions, which could change in the future as our plans and business conditions evolve. The amounts and timing of our actual expenditures depend on numerous factors, including the progress of our preclinical development efforts, the ongoing status of and results of our clinical trials and other studies and any unforeseen cash needs. As a result, our management will have broad discretion in the application of the net proceeds, and investors will be relying on the judgment of our management regarding the application of the net proceeds of this offering. Although we may use a portion of the net proceeds from the offering for the acquisition or licensing, as the case may be, of product candidates, technologies, compounds, other assets or complementary businesses, we have no current understandings, agreements or commitments to do so. Pending these uses, we intend to invest the net proceeds from this offering in interest-bearing, investment-grade securities.

Capitalization

The following table sets forth our cash and cash equivalents and our capitalization as of September 30, 2020 on:

- an actual basis; and
- an as adjusted basis to give effect to the issuance and sale by us of 4,266,211 shares of common stock in this offering at an assumed public price of \$23.44 per share (the last reported sale price of our common stock on the Nasdaq Global Market on December 9, 2020), after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

The information in the table below is illustrative only, and our capitalization following the completion of this offering and the concurrent offering, if it is completed, will depend on the final terms of the offering. The following information should be read in conjunction with the consolidated financial statements and related notes incorporated by reference in this prospectus supplement and the accompanying prospectus. For more details on how you can obtain the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, see “Where You Can Find More Information” and “Incorporation of Certain Information by Reference.” The following table assumes no exercise of the underwriters’ option to purchase additional shares in this offering.

	As of September 30, 2020	
	Actual	As adjusted
	(in thousands, except share and per share data)	
Cash, cash equivalents and marketable securities	\$ 199,999	\$ 293,394
Stockholders’ equity:		
Common stock, \$0.00001 par value, 90,000,000 authorized; issued and outstanding, 37,314,873 actual and 41,581,084 as adjusted	—	—
Additional paid-in capital	434,603	527,998
Accumulated other comprehensive loss	(88)	(88)
Accumulated deficit	(264,925)	(264,925)
Total stockholders’ equity	169,590	262,985
Total capitalization	\$ 169,590	\$ 262,985

The number of shares of our common stock shown as issued and outstanding in the table above is based on shares of our common stock outstanding as of September 30, 2020 and excludes:

- 3,480,141 shares of common stock issuable upon the exercise of stock options issued and outstanding under the 2016 Plan, as of September 30, 2020, having a weighted average exercise price of \$12.63 per share;
- 262,608 shares of common stock issuable upon the vesting of outstanding restricted stock units, under the 2016 Plan, as of September 30, 2020;
- an aggregate of 552,511 shares of common stock, subject to increase on an annual basis, reserved for future issuance under the 2016 Plan, as of September 30, 2020;
- 603,500 shares of common stock issuable upon the exercise of stock options issued and outstanding under the Inducement Plan, as of September 30, 2020, having a weighted average exercise price of \$11.64 per share;
- an aggregate of 630,000 shares of common stock reserved for future issuance under the Inducement Plan, as of September 30, 2020;
- 513,178 shares of common stock issuable upon the exercise of stock options issued and outstanding under our 2007 Equity Incentive Plan, as of September 30, 2020, having a weighted average exercise price of \$3.43 per share;

- 757,647 shares of our common stock reserved for future issuance under our 2016 Employee Stock Purchase Plan, as of September 30, 2020;
- 2,750,000 shares of common stock issuable upon the exercise of warrants outstanding as of September 30, 2020, 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, 2020, at a weighted average exercise price of \$0.00001 per share.

Subsequent to September 30, 2020, and through the date of this prospectus supplement, we issued and sold an aggregate of 917,879 shares of common stock at an average price of \$21.03 per share pursuant to our at-the-market offering program. The number of shares of common stock to be outstanding immediately following this offering as described herein does not include such shares sold pursuant to our at-the-market offering program.

Dilution

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

Our net tangible book value as of September 30, 2020 was approximately \$169.6 million, or \$4.54 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, 2020. 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 issuance and sale of 4,266,211 shares of our common stock in this offering at an assumed public offering price of \$23.44 per share, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our as adjusted net tangible book value as of September 30, 2020 would have been approximately \$263.0 million, or \$6.32 per share. This represents an immediate increase in net tangible book value of \$1.78 per share to existing stockholders and immediate dilution of \$17.12 per share to investors purchasing our common stock in this offering at the public offering price. The following table illustrates this dilution on a per share basis:

Assumed public offering price per share	\$23.44
Net tangible book value per share as of September 30, 2020	\$4.54
Increase in net tangible book value per share attributable to this offering	\$1.78
As adjusted net tangible book value per share as of September 30, 2020, after giving effect to this offering	\$ 6.32
Dilution per share to new investors purchasing our common stock in this offering	\$17.12

The above discussion and table are based on 37,314,873 shares of our common stock outstanding as of September 30, 2020 and excludes:

- 3,480,141 shares of common stock issuable upon the exercise of stock options issued and outstanding under the 2016 Plan, as of September 30, 2020, having a weighted average exercise price of \$12.63 per share;
- 262,608 shares of common stock issuable upon the vesting of outstanding restricted stock units, under the 2016 Plan, as of September 30, 2020;
- an aggregate of 552,511 shares of common stock, subject to increase on an annual basis, reserved for future issuance under the 2016 Plan, as of September 30, 2020;
- 603,500 shares of common stock issuable upon the exercise of stock options issued and outstanding under the Inducement Plan, as of September 30, 2020, having a weighted average exercise price of \$11.64 per share;
- an aggregate of 630,000 shares of common stock reserved for future issuance under the Inducement Plan, as of September 30, 2020;
- 513,178 shares of common stock issuable upon the exercise of stock options issued and outstanding under our 2007 Equity Incentive Plan, as of September 30, 2020, having a weighted average exercise price of \$3.43 per share;
- 757,647 shares of our common stock reserved for future issuance under our 2016 Employee Stock Purchase Plan, as of September 30, 2020;
- 2,750,000 shares of common stock issuable upon the exercise of warrants outstanding as of September 30, 2020, 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, 2020, at a weighted average exercise price of \$0.00001 per share.

Subsequent to September 30, 2020, and through the date of this prospectus supplement, we issued and sold an aggregate of 917,879 shares of common stock at an average price of \$21.03 per share pursuant to our at-the-market offering program. The number of shares of common stock to be outstanding immediately following this offering as described herein does not include such shares sold pursuant to our at-the-market offering program.

To the extent that options or warrants outstanding as of September 30, 2020 have been or may be exercised or other shares issued, investors purchasing our common stock in this offering may experience further dilution. In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of these securities could result in further dilution to our stockholders.

Material U.S. federal income tax consequences to non-U.S. holders

The following is a discussion of the material U.S. federal income tax considerations applicable to non-U.S. holders (as defined below) with respect to their ownership and disposition of shares of our common stock issued pursuant to this offering, but does not purport to be a complete analysis of all potential tax effects. All prospective non-U.S. holders of our common stock should consult their own tax advisors with respect to the U.S. federal income tax consequences of the purchase, ownership and disposition of our common stock, as well as any consequences arising under the laws of any other taxing jurisdiction, including any state, local and non-U.S. tax consequences and any U.S. federal non-income tax consequences. In general, a non-U.S. holder means a beneficial owner of our common stock (other than a partnership or an entity or arrangement treated as a partnership for U.S. federal income tax purposes) that is not, for U.S. federal income tax purposes:

- an individual who is a citizen or resident of the United States;
- a corporation, or an entity treated as a corporation for U.S. federal income tax purposes, created or organized in the United States or under the laws of the United States or of any state thereof or the District of Columbia;
- an estate, the income of which is subject to U.S. federal income tax regardless of its source; or
- a trust if (1) a U.S. court can exercise primary supervision over the trust's administration and one or more U.S. persons have the authority to control all of the trust's substantial decisions or (2) the trust has a valid election in effect under applicable U.S. Treasury Regulations to be treated as a U.S. person.

This discussion is based on current provisions of the U.S. Internal Revenue Code of 1986, as amended, which we refer to as the Code, existing U.S. Treasury Regulations promulgated thereunder, published administrative rulings and judicial decisions, all as in effect as of the date of this prospectus supplement. These laws are subject to change and to differing interpretation, possibly with retroactive effect. Any change or differing interpretation could alter the tax consequences to non-U.S. holders described in this prospectus supplement.

This discussion is limited to non-U.S. holders that hold shares of our common stock as a capital asset within the meaning of Section 1221 of the Code (generally, for investment). This discussion does not address all aspects of U.S. federal income taxation that may be relevant to a particular non-U.S. holder in light of that non-U.S. holder's individual circumstances, nor does it address any aspects of U.S. estate or gift tax, or any state, local or non-U.S. taxes. This discussion also does not consider any specific facts or circumstances that may apply to a non-U.S. holder and does not address the special tax rules applicable to particular non-U.S. holders, such as holders that own, or are deemed to own, more than 5% of our capital stock (except to the extent specifically set forth below), corporations that accumulate earnings to avoid U.S. federal income tax, tax-exempt organizations, banks, financial institutions, insurance companies, brokers, dealers or traders in securities, commodities or currencies, tax-qualified retirement plans, holders subject to the alternative minimum tax or Medicare contribution tax, holders who hold or receive our common stock pursuant to the exercise of employee stock options or otherwise as compensation, holders holding our common stock as part of a hedge, straddle or other risk reduction strategy, conversion transaction or other integrated investment, holders deemed to sell our common stock under the constructive sale provisions of the Code, persons subject to special tax accounting rules under Section 451(b) of the Code, "qualified foreign pension funds" as defined in Section 897(l)(2) of the Code and entities all of the interests of which are held by qualified foreign pension funds, controlled foreign corporations, passive foreign investment companies and U.S. expatriates and certain former citizens or long-term residents of the United States.

In addition, this discussion does not address the tax treatment of partnerships (or entities or arrangements that are treated as partnerships for U.S. federal income tax purposes) or persons that hold their common stock through such partnerships or such entities or arrangements. If a partnership, including any entity or arrangement treated as a partnership for U.S. federal income tax purposes, holds shares of our common stock, the U.S. federal income tax treatment of a partner in such partnership will generally depend upon the status of the partner, the activities of the partnership and certain determinations made at the partner level. Such partners and partnerships should consult their own tax advisors regarding the tax consequences of the purchase, ownership and disposition of our common stock.

There can be no assurance that the Internal Revenue Service, which we refer to as the IRS, will not challenge one or more of the tax consequences described herein, and we have not obtained, nor do we intend to obtain, a ruling with respect to the U.S. federal income tax consequences with respect to the matters discussed below.

Distributions on our common stock

Distributions, if any, on our common stock generally will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. If a distribution exceeds our current and accumulated earnings and profits, the excess will be treated as a tax-free return of the non-U.S. holder's investment, up to such holder's adjusted tax basis in the common stock. Any remaining excess will be treated as capital gain from the sale or exchange of such common stock, subject to the tax treatment described below in "Gain on Sale, Exchange or Other Disposition of Our Common Stock."

Subject to the discussion below regarding backup withholding and foreign accounts, dividends paid to a non-U.S. holder will generally be subject to withholding of U.S. federal income tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty. A non-U.S. holder that is eligible for a reduced rate of U.S. withholding tax under an income tax treaty may obtain a refund or credit of any excess amounts withheld by timely filing an appropriate claim for refund with the IRS. A non-U.S. holder of our common stock who claims the benefit of an applicable income tax treaty generally will be required to provide a properly executed IRS Form W-8BEN or W-8BEN-E (or successor form) and satisfy relevant certification and other requirements. Non-U.S. holders are urged to consult their tax advisors regarding their entitlement to benefits under a relevant income tax treaty.

Dividends that are treated as effectively connected with a trade or business conducted by a non-U.S. holder within the United States and, if an applicable income tax treaty so provides, that are attributable to a permanent establishment or a fixed base maintained by the non-U.S. holder within the United States are generally exempt from the 30% withholding tax if the non-U.S. holder satisfies applicable certification and disclosure requirements. To claim the exemption, the non-U.S. holder must furnish to us or the applicable withholding agent a valid IRS Form W-8ECI (or applicable successor form), certifying that the dividends are effectively connected with the non-U.S. holder's conduct of a trade or business within the United States. However, such U.S. effectively connected income, net of specified deductions and credits, is taxed at the same U.S. federal income tax rates applicable to U.S. persons (as defined in the Code), unless a specific treaty exemption applies. Any U.S. effectively connected income received by a non-U.S. holder that is a corporation may also, under certain circumstances, be subject to an additional "branch profits tax" at a 30% rate or such lower rate as may be specified by an applicable income tax treaty.

Gain on sale, exchange or other disposition of our common stock

Subject to the discussions below regarding backup withholding and foreign accounts, in general, a non-U.S. holder will not be subject to any U.S. federal income tax on any gain realized upon such holder's sale, exchange or other disposition of shares of our common stock unless:

- the gain is effectively connected with a U.S. trade or business of the non-U.S. holder and, if an applicable income tax treaty so provides, is attributable to a permanent establishment or a fixed base maintained in the United States by such non-U.S. holder, in which case the non-U.S. holder generally will be taxed at the U.S. federal income tax rates applicable to U.S. persons (as defined in the Code) and, if the non-U.S. holder is a foreign corporation, the branch profits tax described above in "Distributions on Our Common Stock" may also apply;
- the non-U.S. holder is a nonresident alien individual who is present in the United States for 183 days or more in the taxable year of the disposition and certain other conditions are met, in which case the non-U.S. holder will be subject to a 30% tax (or such lower rate as may be specified by an applicable income tax treaty) on the net gain derived from the disposition, which may be offset by U.S. source capital losses of the non-U.S. holder, if any (even though the individual is not considered a resident of the United States), provided the non-U.S. holder has timely filed U.S. federal income tax returns with respect to such losses; or

- our common stock constitutes a U.S. real property interest because we are, or have been, at any time during the five-year period preceding such disposition (or the non-U.S. holder's holding period, if shorter) a "U.S. real property holding corporation." Even if we are or become a U.S. real property holding corporation, provided that our common stock is regularly traded on an established securities market, our common stock will be treated as a U.S. real property interest only with respect to a non-U.S. holder that holds more than 5% of our outstanding common stock, directly or indirectly, actually or constructively, during the shorter of the five-year period ending on the date of the disposition or the period that the non-U.S. holder held our common stock. In such case, such non-U.S. holder generally will be taxed on its net gain derived from the disposition at the U.S. federal income tax rates applicable to U.S. persons (as defined in the Code). Generally, a corporation is a U.S. real property holding corporation only if the fair market value of its U.S. real property interests equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests plus its other assets used or held for use in a trade or business. Although there can be no assurance, we do not believe that we are, or have been, a U.S. real property holding corporation, or that we are likely to become one in the future. No assurance can be provided that our common stock will be regularly traded on an established securities market for purposes of the rules described above.

Backup withholding and information reporting

We must report annually to the IRS and to each non-U.S. holder the gross amount of the dividends on our common stock paid to such holder and the tax withheld, if any, with respect to such dividends. Non-U.S. holders will have to comply with specific certification procedures to establish that the holder is not a U.S. person (as defined in the Code) in order to avoid backup withholding at the applicable rate with respect to dividends on our common stock. U.S. backup withholding generally will not apply to a non-U.S. holder who provides a properly executed IRS Form W-8BEN or W-8BEN-E or otherwise establishes an exemption.

Information reporting and backup withholding will generally apply to the proceeds of a disposition of our common stock by a non-U.S. holder effected by or through the U.S. office of any broker, U.S. or foreign, unless the holder certifies its status as a non-U.S. holder and satisfies certain other requirements, or otherwise establishes an exemption. Generally, information reporting and backup withholding will not apply to a payment of disposition proceeds to a non-U.S. holder where the transaction is effected outside the United States through a non-U.S. office of a broker. However, for information reporting purposes, dispositions effected through a non-U.S. office of a broker with substantial U.S. ownership or operations generally will be treated in a manner similar to dispositions effected through a U.S. office of a broker.

Non-U.S. holders should consult their own tax advisors regarding the application of the information reporting and backup withholding rules to them.

Copies of information returns may be made available to the tax authorities of the country in which the non-U.S. holder resides or is incorporated under the provisions of a specific treaty or agreement.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules from a payment to a non-U.S. holder may be allowed as a credit against the non-U.S. holder's U.S. federal income tax liability, if any, and may entitle such holder to a refund, provided that the required information is timely furnished to the IRS.

Foreign accounts

Sections 1471 through 1474 of the Code (commonly referred to as FATCA) generally impose a U.S. federal withholding tax of 30% on dividends and, subject to the discussion on the proposed regulations below, the gross proceeds of a disposition of our common stock paid to a "foreign financial institution" (as specifically defined for this purpose), unless such institution enters into an agreement with the U.S. government to, among other things, withhold on certain payments and to collect and provide to the U.S. tax authorities certain information regarding U.S. account holders of such institution (which may include certain equity and debt holders of such institution, as well as certain account holders that are foreign entities with U.S. owners). Foreign financial

institutions located in jurisdictions that have an intergovernmental agreement with the United States governing these withholding and reporting requirements may be subject to different rules. FATCA also generally imposes a 30% withholding tax on dividends, subject to the discussion on the proposed regulations below, and the gross proceeds of a disposition of our common stock paid to a non-financial foreign entity, unless such entity provides the withholding agent with either a certification that it does not have any substantial direct or indirect U.S. owners or information regarding substantial direct and indirect U.S. owners of the entity. The withholding tax described above will not apply if the foreign financial institution or non-financial foreign entity otherwise qualifies for an exemption from the rules. The withholding provisions described above currently apply to dividends on our common stock. The U.S. Treasury Department has released proposed regulations which, if finalized in their present form, would eliminate the federal withholding tax of 30% applicable to the gross proceeds of a disposition of our common stock. In its preamble to such proposed regulations, the U.S. Treasury Department stated that taxpayers may generally rely on the proposed regulations until final regulations are issued.

Under certain circumstances, a non-U.S. holder might be eligible for refunds or credits of such taxes. Non-U.S. holders are encouraged to consult with their own tax advisors regarding the possible implications of the legislation on their investment in our common stock.

EACH PROSPECTIVE INVESTOR SHOULD CONSULT ITS OWN TAX ADVISOR REGARDING THE TAX CONSEQUENCES OF PURCHASING, HOLDING AND DISPOSING OF OUR COMMON STOCK, INCLUDING THE CONSEQUENCES OF ANY PROPOSED CHANGE IN APPLICABLE LAW, AS WELL AS TAX CONSEQUENCES ARISING UNDER ANY STATE, LOCAL, NON-U.S. OR U.S. FEDERAL NON-INCOME TAX LAWS.

Underwriting

We are offering the shares of common stock described in this prospectus through a number of underwriters. J.P. Morgan Securities LLC, SVB Leerink LLC and Piper Sandler & Co. are acting as joint book-running managers of the offering and as representatives of the underwriters. We have entered into an underwriting agreement with the underwriters. Subject to the terms and conditions of the underwriting agreement, we have agreed to sell to the underwriters, and each underwriter has severally agreed to purchase, at the public offering price less the underwriting discounts and commissions set forth on the cover page of this prospectus, the number of shares of common stock listed next to its name in the following table:

Name	Number of shares
J.P. Morgan Securities LLC	
SVB Leerink LLC	
Piper Sandler & Co.	
BMO Capital Markets Corp	
Total	

The underwriters are committed to purchase all the common shares offered by us if they purchase any shares. The underwriting agreement also provides that if an underwriter defaults, the purchase commitments of non-defaulting underwriters may also be increased or the offering may be terminated.

The underwriters propose to offer the common shares directly to the public at the initial public offering price set forth on the cover page of this prospectus and to certain dealers at that price less a concession not in excess of \$ _____ per share. Any such dealers may resell shares to certain other brokers or dealers at a discount of up to \$ _____ per share from the initial public offering price. After the initial offering of the shares to the public, if all of the common shares are not sold at the initial public offering price, the underwriters may change the offering price and the other selling terms. Sales of any shares made outside of the United States may be made by affiliates of the underwriters.

The underwriters have an option to buy up to \$15,000,000 of additional shares of common stock from us. The underwriters have 30 days from the date of this prospectus to exercise this option to purchase additional shares. If any shares are purchased with this option to purchase additional shares, the underwriters will purchase shares in approximately the same proportion as shown in the table above. If any additional shares of common stock are purchased, the underwriters will offer the additional shares on the same terms as those on which the shares are being offered.

The underwriting fee is equal to the public offering price per share of common stock less the amount paid by the underwriters to us per share of common stock. The underwriting fee is \$ _____ per share. The following table shows the per share and total underwriting discounts and commissions to be paid to the underwriters assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

	Without option to purchase additional shares exercise	With full option to purchase additional shares exercise
Per Share	\$	\$
Total	\$	\$

Pursuant to the terms of the underwriting agreement, we have agreed to reimburse the underwriters for certain expenses, including reasonable fees and expenses of counsel, relating to certain aspects of this offering in an amount up to \$25,000. We estimate that the total expenses of this offering, including registration, filing and listing

fees, printing fees and legal and accounting expenses, but excluding the underwriting discounts and commissions, will be approximately \$.

A prospectus in electronic format may be made available on the web sites maintained by one or more underwriters, or selling group members, if any, participating in the offering. The underwriters may agree to allocate a number of shares to underwriters and selling group members for sale to their online brokerage account holders. Internet distributions will be allocated by the representatives to underwriters and selling group members that may make Internet distributions on the same basis as other allocations.

We, our executive officers, and directors have agreed, subject to specified exceptions, not to directly or indirectly:

- sell, offer, contract or grant any option to sell (including any short sale), pledge, transfer, establish an open “put equivalent position” within the meaning of Rule 16a-1(h) under the Securities Exchange Act of 1934, as amended, or
- otherwise dispose of any shares of common stock, options or warrants to acquire shares of common stock, or securities exchangeable or exercisable for or convertible into shares of common stock currently or hereafter owned either of record or beneficially, or
- publicly announce an intention to do any of the foregoing for a period of 90 days after the date of this prospectus supplement without the prior written consent of J.P. Morgan Securities LLC.

This restriction terminates after the close of trading of the common stock on and including the 90th day after the date of this prospectus supplement.

J.P. Morgan Securities LLC may, in its sole discretion and at any time or from time to time before the termination of the 90-day period release all or any portion of the securities subject to lock-up agreements. Except for customary lock-up exceptions, there are no existing agreements between the underwriters and any of our shareholders who will execute a lock-up agreement, providing consent to the sale of shares prior to the expiration of the lock-up period.

Record holders of our securities are typically the parties to the lock-up agreements with the underwriters referred to above, while holders of beneficial interests in our shares who are not also record holders in respect of such shares are not typically subject to any such agreements or other similar restrictions. Accordingly, we believe that certain holders of beneficial interests who are not record holders and are not bound by lock-up agreements could enter into transactions with respect to those beneficial interests that negatively impact our stock price. In addition, a shareholder who is not subject to a lock-up agreement with the underwriters may be able to sell, short sell, transfer, hedge, pledge, lend or otherwise dispose of or attempt to sell short sell, transfer, hedge, pledge, lend or otherwise dispose of, their equity interests at any time after the closing of this offering.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act of 1933.

Our common stock is listed on the Nasdaq Global Market under the symbol “PTGX.”

In connection with this offering, the underwriters may engage in stabilizing transactions, which involves making bids for, purchasing and selling shares of common stock in the open market for the purpose of preventing or retarding a decline in the market price of the common stock while this offering is in progress. These stabilizing transactions may include making short sales of common stock, which involves the sale by the underwriters of a greater number of shares of common stock than they are required to purchase in this offering, and purchasing shares of common stock on the open market to cover positions created by short sales. Short sales may be “covered” shorts, which are short positions in an amount not greater than the underwriters’ option to purchase additional shares referred to above, or may be “naked” shorts, which are short positions in excess of that amount. The underwriters may close out any covered short position either by exercising their option to purchase additional shares, in whole or in part, or by purchasing shares in the open market. In making this determination, the underwriters will consider, among other things, the price of shares available for purchase in the open

market compared to the price at which the underwriters may purchase shares through the option to purchase additional shares. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market that could adversely affect investors who purchase in this offering. To the extent that the underwriters create a naked short position, they will purchase shares in the open market to cover the position.

The underwriters have advised us that, pursuant to Regulation M of the Securities Act of 1933, they may also engage in other activities that stabilize, maintain or otherwise affect the price of the common stock, including the imposition of penalty bids. This means that if the representatives of the underwriters purchase common stock in the open market in stabilizing transactions or to cover short sales, the representatives can require the underwriters that sold those shares as part of this offering to repay the underwriting discount received by them.

These activities may have the effect of raising or maintaining the market price of the common stock or preventing or retarding a decline in the market price of the common stock, and, as a result, the price of the common stock may be higher than the price that otherwise might exist in the open market. If the underwriters commence these activities, they may discontinue them at any time. The underwriters may carry out these transactions on the Nasdaq Global Market, in the over-the-counter market or otherwise.

Other than in the United States, no action has been taken by us or the underwriters that would permit a public offering of the securities offered by this prospectus in any jurisdiction where action for that purpose is required. The securities offered by this prospectus may not be offered or sold, directly or indirectly, nor may this prospectus or any other offering material or advertisements in connection with the offer and sale of any such securities be distributed or published in any jurisdiction, except under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons into whose possession this prospectus comes are advised to inform themselves about and to observe any restrictions relating to the offering and the distribution of this prospectus. This prospectus does not constitute an offer to sell or a solicitation of an offer to buy any securities offered by this prospectus in any jurisdiction in which such an offer or a solicitation is unlawful.

Notice to prospective investors in the European Economic Area and the United Kingdom

In relation to each Member State of the European Economic Area and the United Kingdom (each, a “Relevant State”), no shares have been offered or will be offered pursuant to the offering to the public in that Relevant State prior to the publication of a prospectus in relation to the shares which has been approved by the competent authority in that Relevant State or, where appropriate, approved in another Relevant State and notified to the competent authority in that Relevant State, all in accordance with the Prospectus Regulation, except that offers of shares may be made to the public in that Relevant State at any time under the following exemptions under the Prospectus Regulation:

- A. to any legal entity which is a qualified investor as defined under the Prospectus Regulation;
- B. to fewer than 150 natural or legal persons (other than qualified investors as defined under the Prospectus Regulation), subject to obtaining the prior consent of the underwriters; or
- C. in any other circumstances falling within Article 1(4) of the Prospectus Regulation, provided that no such offer of shares shall require us or any underwriter to publish a prospectus pursuant to Article 3 of the Prospectus Regulation or supplement a prospectus pursuant to Article 23 of the Prospectus Regulation and each person who initially acquires any shares or to whom any offer is made will be deemed to have represented, acknowledged and agreed to and with us and each of the underwriters that it is a “qualified investor” within the meaning of Article 2(e) of the Prospectus Regulation.

In the case of any shares being offered to a financial intermediary as that term is used in the Prospectus Regulation, each such financial intermediary will be deemed to have represented, acknowledged and agreed that the shares acquired by it in the offer have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in circumstances which may give rise to an offer

of any shares to the public other than their offer or resale in a Relevant State to qualified investors as so defined or in circumstances in which the prior consent of the underwriters has been obtained to each such proposed offer or resale.

For the purposes of this provision, the expression an “offer to the public” in relation to shares in any Relevant State means the communication in any form and by any means of sufficient information on the terms of the offer and any shares to be offered so as to enable an investor to decide to purchase or subscribe for any shares, and the expression “Prospectus Regulation” means Regulation EU 2017/1129.

Notice to prospective investors in the United Kingdom

In addition, in the United Kingdom, this document is being distributed only to, and is directed only at, and any offer subsequently made may only be directed at persons who are “qualified investors” (as defined in the Prospectus Regulation) (i) who have professional experience in matters relating to investments falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended (the “Order”) and/or (ii) who are high net worth companies (or persons to whom it may otherwise be lawfully communicated) falling within Article 49(2)(a) to (d) of the Order (all such persons together being referred to as “relevant persons”) or otherwise in circumstances which have not resulted and will not result in an offer to the public of the shares in the United Kingdom within the meaning of the Financial Services and Markets Act 2000.

Any person in the United Kingdom that is not a relevant person should not act or rely on the information included in this document or use it as basis for taking any action. In the United Kingdom, any investment or investment activity that this document relates to may be made or taken exclusively by relevant persons.

Notice to prospective investors in Canada

The shares may be sold only to purchasers purchasing, or deemed to be purchasing, as principal that are accredited investors, as defined in National Instrument 45-106 Prospectus Exemptions or subsection 73.3(1) of the Securities Act (Ontario), and are permitted clients, as defined in National Instrument 31-103 Registration Requirements, Exemptions and Ongoing Registrant Obligations. Any resale of the shares must be made in accordance with an exemption from, or in a transaction not subject to, the prospectus requirements of applicable securities laws.

Securities legislation in certain provinces or territories of Canada may provide a purchaser with remedies for rescission or damages if this prospectus (including any amendment thereto) contains a misrepresentation, provided that the remedies for rescission or damages are exercised by the purchaser within the time limit prescribed by the securities legislation of the purchaser’s province or territory. The purchaser should refer to any applicable provisions of the securities legislation of the purchaser’s province or territory for particulars of these rights or consult with a legal advisor.

Pursuant to section 3A.3 of National Instrument 33-105 Underwriting Conflicts (NI 33-105), the underwriters are not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

Notice to prospective investors in Switzerland

The shares may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange (“SIX”) or on any other stock exchange or regulated trading facility in Switzerland. This document does not constitute a prospectus within the meaning of, and has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this document nor any other offering or marketing material relating to the shares or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this document nor any other offering or marketing material relating to the offering, us, or the shares have been or will be filed with or approved by any Swiss regulatory authority. In particular, this document will not

be filed with, and the offer of shares will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA (FINMA), and the offer of shares has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes (“CISA”). The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of shares.

Notice to prospective investors in Australia

This prospectus supplement:

- does not constitute a disclosure document or a prospectus under Chapter 6D.2 of the Corporations Act 2001 (Cth) (the “Corporations Act”);
- has not been, and will not be, lodged with the Australian Securities and Investments Commission (“ASIC”), as a disclosure document for the purposes of the Corporations Act and does not purport to include the information required of a disclosure document for the purposes of the Corporations Act; and
- may only be provided in Australia to select investors who are able to demonstrate that they fall within one or more of the categories of investors available under section 708 of the Corporations Act (“Exempt Investors”).

The shares may not be directly or indirectly offered for subscription or purchased or sold, and no invitations to subscribe for or buy the shares may be issued, and no draft or definitive offering memorandum, advertisement or other offering material relating to any shares may be distributed in Australia, except where disclosure to investors is not required under Chapter 6D of the Corporations Act or is otherwise in compliance with all applicable Australian laws and regulations. By submitting an application for the shares, you represent and warrant to us that you are an Exempt Investor.

As any offer of shares under this document will be made without disclosure in Australia under Chapter 6D.2 of the Corporations Act, the offer of those securities for resale in Australia within 12 months may, under section 707 of the Corporations Act, require disclosure to investors under Chapter 6D.2 if none of the exemptions in section 708 applies to that resale. By applying for the shares you undertake to us that you will not, for a period of 12 months from the date of issue of the shares, offer, transfer, assign or otherwise alienate those shares to investors in Australia except in circumstances where disclosure to investors is not required under Chapter 6D.2 of the Corporations Act or where a compliant disclosure document is prepared and lodged with ASIC.

Notice to prospective investors in Japan

The shares have not been and will not be registered pursuant to Article 4, Paragraph 1 of the Financial Instruments and Exchange Act. Accordingly, none of the shares nor any interest therein may be offered or sold, directly or indirectly, in Japan or to, or for the benefit of, any “resident” of Japan (which term as used herein means any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to or for the benefit of a resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the Financial Instruments and Exchange Act and any other applicable laws, regulations and ministerial guidelines of Japan in effect at the relevant time.

Notice to prospective investors in Hong Kong

The shares have not been offered or sold and will not be offered or sold in Hong Kong, by means of any document, other than (a) to “professional investors” as defined in the Securities and Futures Ordinance (Cap. 571 of the Laws of Hong Kong) (the “SFO”) of Hong Kong and any rules made thereunder; or (b) in other circumstances which do not result in the document being a “prospectus” as defined in the Companies (Winding Up and Miscellaneous Provisions) Ordinance (Cap. 32) of Hong Kong (the “CO”) or which do not constitute an offer to the public within the meaning of the CO. No advertisement, invitation or document relating to the shares has been or may be issued or has been or may be in the possession of any person for the purposes of issue, whether in Hong Kong or elsewhere, which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong

(except if permitted to do so under the securities laws of Hong Kong) other than with respect to shares which are or are intended to be disposed of only to persons outside Hong Kong or only to “professional investors” as defined in the SFO and any rules made thereunder.

Notice to prospective investors in Singapore

Each joint book-running manager has acknowledged that this prospectus supplement has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, each joint book-running manager has represented and agreed that it has not offered or sold any shares or caused the shares to be made the subject of an invitation for subscription or purchase and will not offer or sell any shares or cause the shares to be made the subject of an invitation for subscription or purchase, and has not circulated or distributed, nor will it circulate or distribute, this prospectus supplement or any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares, whether directly or indirectly, to any person in Singapore other than (i) to an institutional investor (as defined in Section 4A of the Securities and Futures Act (Chapter 289) of Singapore, as modified or amended from time to time (the “SFA”)) pursuant to Section 274 of the SFA; (ii) to a relevant person (as defined in Section 275(2) of the SFA) pursuant to Section 275(1) of the SFA, or any person pursuant to Section 275(1A) of the SFA, and in accordance with the conditions specified in Section 275 of the SFA, or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the shares are subscribed or purchased under Section 275 of the SFA by a relevant person which is: (a) a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or (b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor, securities or securities-based derivatives contracts (each term as defined in Section 2(1) of the SFA) of that corporation or the beneficiaries’ rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the shares pursuant to an offer made under Section 275 of the SFA except:

- (a) to an institutional investor or to a relevant person, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;
- (b) where no consideration is or will be given for the transfer;
- (c) where the transfer is by operation of law;
- (d) as specified in Section 276(7) of the SFA; or
- (e) as specified in Regulation 37A of the Securities and Futures (Offers of Investments) Securities and Securities-based Derivatives Contracts) Regulations 2018.

Singapore SFA Product Classification—In connection with Section 309B of the SFA and the CMP Regulations 2018, unless otherwise specified before an offer of the shares, the Issuer has determined, and hereby notifies all relevant persons (as defined in Section 309A(1) of the SFA), that the shares are “prescribed capital markets products” (as defined in the CMP Regulations 2018) and Excluded Investment Products (as defined in MAS Notice SFA 04-N12: Notice on the Sale of Investment Products and MAS Notice FAA-N16: Notice on Recommendations on Investment Products).

Notice to prospective investors in China

This prospectus supplement will not be circulated or distributed in the PRC and the shares will not be offered or sold, and will not be offered or sold to any person for re-offering or resale directly or indirectly to any residents of the PRC except pursuant to any applicable laws and regulations of the PRC. Neither this prospectus supplement

nor any advertisement or other offering material may be distributed or published in the PRC, except under circumstances that will result in compliance with applicable laws and regulations.

Notice to prospective investors in the Dubai International Financial Centre

This prospectus supplement relates to an Exempt Offer in accordance with the Markets Rules 2012 of the Dubai Financial Services Authority (“DFSA”). This prospectus supplement is intended for distribution only to persons of a type specified in the Markets Rules 2012 of the DFSA. It must not be delivered to, or relied on by, any other person. The DFSA has no responsibility for reviewing or verifying any documents in connection with Exempt Offers. The DFSA has not approved this prospectus supplement nor taken steps to verify the information set forth herein and has no responsibility for the prospectus supplement. The shares to which this prospectus supplement relates may be illiquid and/or subject to restrictions on their resale. Prospective purchasers of the shares offered should conduct their own due diligence on the shares. If you do not understand the contents of this prospectus supplement you should consult an authorized financial advisor.

In relation to its use in the DIFC, this document is strictly private and confidential and is being distributed to a limited number of investors and must not be provided to any person other than the original recipient, and may not be reproduced or used for any other purpose. The interests in the shares may not be offered or sold directly or indirectly to the public in the DIFC.

Certain of the underwriters and their affiliates have provided in the past to us and our affiliates and may provide from time to time in the future certain commercial banking, financial advisory, investment banking and other services for us and such affiliates in the ordinary course of their business, for which they have received and may continue to receive customary fees and commissions. In addition, from time to time, certain of the underwriters and their affiliates may effect transactions for their own account or the account of customers, and hold on behalf of themselves or their customers, long or short positions in our debt or equity securities or loans, and may do so in the future.

Legal matters

Cooley LLP, Palo Alto, California will pass upon the validity of the shares of common stock offered hereby. The underwriters are being represented by Latham & Watkins LLP, San Diego, California, in connection with the offering.

Experts

The financial statements incorporated in this prospectus supplement by reference to the [Annual Report on Form 10-K for the year ended December 31, 2019](#) 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 on Form S-3ASR we filed with the SEC under the Securities Act and does not contain all the information set forth in the registration statement. Whenever a reference is made in this prospectus supplement or the accompanying prospectus to any of our contracts, agreements or other documents, the reference may not be complete and you should refer to the exhibits that are a part of the registration statement or the exhibits to the reports or other documents incorporated by reference therein. For further information with respect to us and the common stock we are offering under this prospectus supplement, we refer you to the registration statement and the exhibits and schedules filed as a part of the registration statement. Because we are subject to the information and reporting requirements of the Securities Exchange Act of 1934 (the "Exchange Act"), we file annual, quarterly and current reports, proxy statements and other information with the SEC. Our SEC filings are available to the public over the internet 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:

- our [Annual Report on Form 10-K for the year ended December 31, 2019, filed with the SEC on March 10, 2020](#), including the information specifically incorporated by reference therein from our [definitive proxy statement on Schedule 14A, filed with the SEC on April 16, 2020](#);
- our [Quarterly Report on Form 10-Q for the quarter ended March 31, 2020, filed with the SEC on May 7, 2020](#);
- our [Quarterly Report on Form 10-Q for the quarter ended June 30, 2020, filed with the SEC on August 6, 2020](#);
- our [Quarterly Report on Form 10-Q for the quarter ended September 30, 2020, filed with the SEC on November 4, 2020](#);
- our current reports on Form 8-K, filed with the SEC on [February 24, 2020](#), [March 18, 2020](#), [May 7, 2020 \(Item 8.01\)](#), [May 12, 2020](#), [May 29, 2020](#), [August 13, 2020](#) (as amended by our current report on Form 8-K/A filed on [October 2, 2020](#)), [September 11, 2020](#), and [November 4, 2020 \(Item 8.01\)](#); 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, including [Exhibit 4.7 to our Annual Report on Form 10-K for the fiscal year ended December 31, 2019 filed with the SEC on March 10, 2020](#).

All filings filed by us pursuant to the Exchange Act after the date of the initial filing of the registration statement of which this prospectus supplement is a part effective upon filing shall be deemed to be incorporated by reference into this prospectus.

We also incorporate by reference any future filings (other than current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items unless such Form 8-K expressly provides to the contrary) made with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, until we file a post-effective amendment that indicates the termination of the offering of the securities made by this prospectus and will become a part of this prospectus from the date that such documents are filed with the SEC. Information in such future filings updates and supplements the information provided in this prospectus. Any statements in any such future filings will automatically be deemed to modify and supersede any information in any document we previously filed with the SEC that is incorporated or deemed to be incorporated herein by reference to the extent that statements in the later filed document modify or replace such earlier statements.

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



Common Stock
Preferred Stock
Debt Securities
Warrants

We may, from time to time, offer and sell 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 the 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 or agents are involved in the sale of any securities with respect to which this prospectus is being delivered, the names of such underwriters or agents and any applicable fees, discounts or commissions and options to purchase additional securities will be set forth in a prospectus supplement. The price to the public of such securities and the net proceeds we expect to receive from such sale will also be set forth in a prospectus supplement.

Our common stock is listed on the Nasdaq Global Market under the symbol "PTGX." On December 9, 2020, the last reported sale price of our common stock on the Nasdaq Global Market was \$23.44 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 applicable 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 8 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 December 10, 2020.

TABLE OF CONTENTS

	Page
About this Prospectus	ii
Prospectus Summary	1
The Securities We May Offer	5
Risk Factors	8
Forward-Looking Statements	9
Use of Proceeds	11
Description of Capital Stock	12
Description of Debt Securities	17
Description of Warrants	24
Legal Ownership of Securities	26
Plan of Distribution	29
Legal Matters	31
Experts	31
Where You Can Find More Information	31
Incorporation of Certain Information by Reference	31

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 an automatic registration statement on Form S-3 that we filed with the Securities and Exchange Commission, or SEC, using a “shelf” registration process as a “well-known seasoned issuer” as defined in Rule 405 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 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, in one or more offerings as described in this prospectus. There is no limit on the aggregate amount of the securities that we may offer pursuant to the registration statement of which this prospectus forms a part. 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 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 that 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

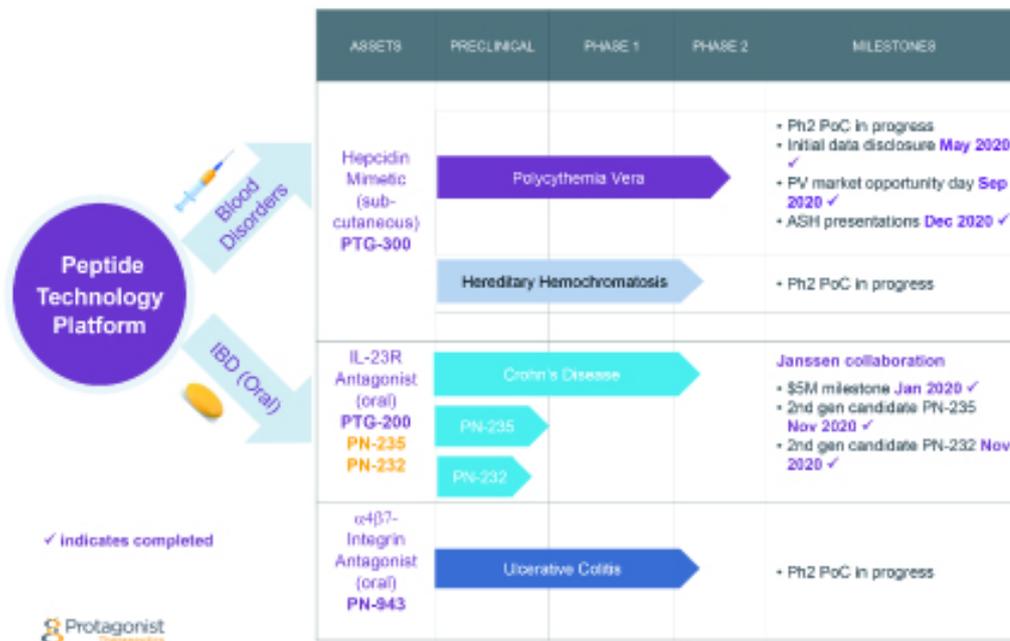
This summary highlights selected information contained elsewhere in this prospectus or incorporated by reference herein and does not contain all of the information that you need to consider in making your investment decision. You should carefully read the entire prospectus, the applicable prospectus 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 that utilizes a proprietary technology platform to discover and develop novel peptide-based drugs to address significant unmet medical needs and transform existing treatment paradigms for patients. We have three assets in various stages of clinical development derived from this platform.

Our Product Pipeline



Our most advanced clinical asset, PTG-300, is an injectable hepcidin mimetic in development for the potential treatment of erythrocytosis, iron overload and other blood disorders. Hepcidin is a key hormone in regulating iron equilibrium and is critical to the proper development of red blood cells. PTG-300 mimics the effect of the natural hormone hepcidin, but with greater potency, solubility and stability. We initiated a Phase 2 proof of concept (“PoC”) study in polycythemia vera (“PV”) in the third quarter of 2019 and a Phase 2 PoC study in hereditary hemochromatosis (“HH”) in January 2020. We believe the interim results from our initial Phase 2 PV efficacy data from a small number of patients provide evidence regarding the potential of PTG-300 to eliminate the need for phlebotomy by controlling hematocrit levels below 45% on an individual patient basis. The American Society for Hematology accepted four posters and one oral presentation relating to PTG-300 for its virtual annual meeting held in December 2020, including updated

Phase 2 results for PTG-300 in PV. PTG-300 has a unique mechanism of action in the potential treatment of PV, which may enable it to decrease and maintain hematocrit levels within the range of recommended clinical guidelines without causing the iron deficiency that may occur with frequent phlebotomy. We have announced the selection of PV as our first indication for a potential pivotal study to begin in 2021. In June 2020, the U.S. Food and Drug Administration (“FDA”) granted orphan drug designation for PTG-300 for the treatment of PV. In December 2020, the FDA granted Fast Track designation for PTG-300 for the treatment of PV. We discontinued development of PTG-300 for anemia associated with beta-thalassemia and myelodysplastic syndromes during the first quarter of 2020 and are redirecting the majority of our PTG-300 efforts to the PV indication, while also continuing our exploration of PTG-300 in HH.

Our clinical assets PTG-200 and PN-943 are orally delivered investigational 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 are designed to block biological pathways currently targeted by marketed injectable antibody drugs. Our orally stable peptide approach may offer 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 oral therapy. As a result, if successfully developed and approved, we believe they may transform the existing treatment paradigm for IBD.

PTG-200 (also referenced as JNJ-67864238) is an investigational, orally delivered gut-restricted Interleukin-23 receptor (“IL-23R”) antagonist for the treatment of IBD. In May 2017, we 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 certain related compounds for all indications, including IBD. The agreement with Janssen was amended in May 2019 to expand the collaboration by supporting efforts towards second-generation IL-23R antagonists, triggering a \$25.0 million milestone payment to us. In January 2020, as part of the expanded research collaboration, we announced the identification and nomination of an orally delivered IL-23R antagonist peptide as a second-generation development candidate, triggering a \$5.0 million milestone payment to us. Janssen initiated a global Phase 2 PoC clinical study for PTG-200 in moderate-to-severe CD in the fourth quarter of 2019. Because of the COVID-19 pandemic, we have suspended guidance on a timeline for PTG-200 Phase 2 study completion. In October 2020, we announced the selection of two second-generation IL-R antagonists for advancement into clinical development, PN-235 (also referenced as JNJ-77242113) and PN-232 (also referenced as JNJ-75105186). The advancement of three different oral co-development candidates provides us with several strategic options for development in multiple indications. We are also continuing our joint research efforts to identify additional IL-23R antagonists.

PN-943 is an investigational, orally delivered, gut-restricted, alpha-4-beta-7 (“ $\alpha 4\beta 7$ ”) specific integrin antagonist. We developed PN-943 as a potentially more potent orally delivered, gut-restricted $\alpha 4\beta 7$ backup compound to PTG-100, our first-generation orally delivered gut-restricted $\alpha 4\beta 7$ inhibitor that was being developed for treatment of IBD. In 2019, we completed a Phase 1 single ascending dose and multiple ascending dose clinical study of PN-943 in healthy volunteers to evaluate safety, pharmacokinetics and pharmacodynamics. The pharmacodynamic results indicated that the administration of PN-943 was well tolerated and showed of target engagement that were suggestive of higher potency for PN-943 as compared to PTG-100. We submitted a U.S. Investigational New Drug application with the FDA for PN-943 in December 2019, which took effect in January 2020, and have initiated a Phase 2 PoC study in UC. In light of the COVID-19 pandemic, we are continuing to review all aspects of the planned Phase 2 study and are suspending guidance on a timeline for study progress and completion.

Our clinical assets are all derived from our proprietary discovery platform. Our platform enables us to engineer novel, structurally constrained peptides that are designed to retain key advantages of both orally delivered small molecules and injectable antibody drugs, in an effort to overcome many of their limitations as therapeutic agents. Importantly, constrained peptides can be designed to potentially 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 potential 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 (the “First Amendment”). 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 First Amendment. During the fourth quarter of 2019, we became eligible to receive a cash payment of \$5.0 million upon the successful nomination of a second-generation development candidate, which we received during the first quarter of 2020.

Impact of COVID-19 on Our Business

We are subject to risks and uncertainties as a result of the COVID-19 pandemic. We are continuing to closely monitor the impact of the COVID-19 pandemic on our business and have taken and continue to take proactive efforts to protect the health and safety of our patients, clinical research staff and employees, and to maintain business continuity. The extent of the impact of the COVID-19 pandemic on our activities is highly uncertain and difficult to predict, as the pandemic and the response to the pandemic continue to rapidly evolve. Capital markets and economies worldwide have also been negatively impacted by the COVID-19 pandemic, and the pandemic has contributed to a global economic recession. Such economic disruption could have a material adverse effect on our business. Policymakers around the globe have responded with fiscal policy actions to support the healthcare industry and economy as a whole. The magnitude and overall effectiveness of these actions remains uncertain.

The severity of the impact of the COVID-19 pandemic on our activities will depend on a number of factors, including, but not limited to, the duration and severity of the pandemic, including the severity of any additional periods of increases or spikes in the number of cases in the areas we and our suppliers operate and areas where our clinical trial sites are located. Accordingly, the extent and severity of the impact on our existing and planned clinical trials and collaboration activities, all of which are uncertain and cannot be predicted. We have experienced delays in our existing and planned clinical trials due to the worldwide impacts of the pandemic. Our future results of operations and liquidity could be adversely impacted by further delays in existing and planned clinical trials and collaboration activities, difficulty in recruiting patients for these clinical trials, supply chain disruptions, the ongoing impact on operating activities and employees and the ongoing impact of any initiatives or programs that we may undertake to address financial and operational challenges. The extent to which the COVID-19 pandemic may materially impact our future financial condition, liquidity or results of operations is uncertain.

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 other securities, 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.

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 related free writing prospectus that we may authorize to be provided to you) related to the series of preferred stock being offered, as well as the complete certificate of designation that contains the terms of the applicable series of preferred stock.

Debt Securities

We may issue debt securities from time to time, in one or more series, as either senior or subordinated debt or as senior or subordinated convertible debt. The senior debt securities will rank equally with any other unsecured and unsubordinated debt. The subordinated debt securities will be subordinate and junior in right of payment, to the extent and in the manner described in the instrument governing the debt, to all of our senior indebtedness. Convertible 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 related 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 offered 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 prospectuses we have authorized for use in connection with a specific offering, we currently intend to use the net proceeds from the sale of the 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 any subsequent Quarterly Reports 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. 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 that we have filed with the SEC that are incorporated by reference herein contain “forward-looking statements” about us and our industry 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 substantial 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 and the documents incorporated by reference herein, including statements regarding our future results of operations, as well as statements regarding industry trends, 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 terminology such as “anticipate,” “believe,” “continue,” “could,” “design,” “estimate,” “expect,” “intend,” “may,” “plan,” “potentially,” “predict,” “project,” “target,” “contemplate,” “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 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, factors 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 any subsequent Quarterly Reports 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 regulatory submissions and achieving regulatory approvals 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;
- 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 expectations with respect to our existing collaboration agreements;
- 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 may 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 potentially available 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 the sale of the securities offered by us hereunder 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

The description below of our capital stock and provisions of our amended and restated certificate of incorporation and amended and restated bylaws are summaries and are qualified by reference to the amended and restated certificate of incorporation and the amended and restated bylaws which are filed as exhibits to the registration statement of which this prospectus is part, and by the applicable provisions of Delaware law.

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, 2020, 37,314,873 shares of common stock were outstanding and no shares of preferred stock were outstanding.

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.

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;
- 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, 2020, (i) stock options to purchase an aggregate of 3,480,141 shares of common stock and 262,608 restricted stock units were outstanding under our 2016 Equity Incentive Plan, or the 2016 Plan, and (ii) an additional 552,511 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, 2020, (i) stock options to purchase an aggregate of 603,500 shares of common stock were outstanding under our 2018 Inducement Plan, as amended, or the Inducement Plan, and (ii) an additional 630,000 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, 2020, stock options to purchase an aggregate of 513,578 shares of common stock were outstanding under our 2007 Stock Option Plan, or the 2007 Plan, and no shares remained available for future issuance under the 2007 Plan.

As of September 30, 2020, no shares of common stock were outstanding under our 2016 Employee Stock Purchase Plan, or the ESPP, and 757,647 shares remained available for future issuance under the ESPP.

As of September 30, 2020, 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 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 form, 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: (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;
- 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;
- additions to or changes in the provisions relating to satisfaction and discharge of the indenture;
- additions to or changes in the provisions relating to the modification of the indenture both with and without the consent of holders of debt securities issued under the indenture;
- the currency of payment of debt securities if other than U.S. dollars and the manner of determining the equivalent amount in U.S. dollars;
- whether interest will be payable in cash or additional debt securities at our or the holders' option and the terms and conditions upon which the election may be made;
- the terms and conditions, if any, upon which we will pay amounts in addition to the stated interest, premium, if any and principal amounts of the debt securities of the series to any holder that is not a "United States person" for federal tax purposes;
- any restrictions on transfer, sale or assignment of the debt securities of the series; and

- any other specific terms, preferences, rights or limitations of, or restrictions on, the debt securities, any other additions or changes in the provisions of the indenture, and any terms that may be required by us or advisable under applicable laws or regulations.

Conversion or Exchange Rights

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

Consolidation, Merger or Sale

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

Events of Default under the Indenture

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

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

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

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

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

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

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

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

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

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

Modification of Indenture; Waiver

We and the trustee may change an indenture without the consent of any holders with respect to specific matters:

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

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

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

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

Discharge

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 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, as amended, 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, to the extent applicable:

- 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;
- 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, depositary 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 depositary on behalf of other financial institutions that participate in the depositary’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 depositary or its participants. Consequently, for securities issued in global form, we will recognize only the depositary as the holder of the securities, and we will make all payments on the securities to the depositary. The depositary 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 depositary 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 depositary’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 depositary 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 depositary 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 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 depositary, 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 depositary 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 depositary's policies, which may change from time to time, will govern payments, transfers, exchanges and other matters relating to an investor's interest in a global security;
- we and any applicable trustee have no responsibility for any aspect of the depositary's actions or for its records of ownership interests in a global security, nor do we or any applicable trustee supervise the depositary in any way;
- the depositary may, and we understand that DTC will, require that those who purchase and sell interests in 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 depositary'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 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 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.

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 overallotment, stabilizing transactions, short covering transactions and penalty bids in accordance with Regulation M under the Securities Exchange Act of 1934, as amended. Overallotment 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.

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 for the year ended December 31, 2019 incorporated in this prospectus by reference to the [Annual Report on Form 10-K for the year ended December 31, 2019](#) 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. You should rely only on information contained in this prospectus or incorporated by reference into this prospectus. 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 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, 2019, filed with the SEC on March 10, 2020](#), including the information specifically incorporated by reference therein from our [definitive proxy statement on Schedule 14A, filed on April 16, 2020](#);
- our [Quarterly Report on Form 10-Q for the quarter ended March 31, 2020, filed with the SEC on May 7, 2020](#);
- our [Quarterly Report on Form 10-Q for the quarter ended June 30, 2020, filed with the SEC on August 6, 2020](#);
- our [Quarterly Report on Form 10-Q for the quarter ended September 30, 2020, filed with the SEC on November 4, 2020](#);
- our current reports on Form 8-K, filed with the SEC on [February 24, 2020](#), [March 18, 2020](#), [May 7, 2020 \(Item 8.01\)](#), [May 12, 2020](#), [May 29, 2020](#), [August 13, 2020](#) (as amended by our current report on Form 8-K/A filed on [October 2, 2020](#)), [September 11, 2020](#) and [November 4, 2020 \(Item 8.01\)](#); 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, including [Exhibit 4.7 to our Annual Report on Form 10-K for the fiscal year ended December 31, 2019, filed with the SEC on March 10, 2020](#).

All filings filed by us pursuant to the Exchange Act after the date of the initial filing of the registration statement of which this prospectus is a part effective upon filing shall be deemed to be incorporated by reference into this prospectus.

We also incorporate by reference any future filings (other than current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items unless such Form 8-K expressly provides to the contrary) made with the SEC pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, until we file a post-effective amendment that indicates the termination of the offering of the securities made by this prospectus and will become a part of this prospectus from the date that such documents are filed with the SEC. Information in such future filings updates and supplements the information provided in this prospectus. Any statements in any such future filings will automatically be deemed to modify and supersede any information in any document we previously filed with the SEC that is incorporated or deemed to be incorporated herein by reference to the extent that statements in the later filed document modify or replace such earlier statements.

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

\$100,000,000



Common stock

Prospectus supplement

Joint Book-running Managers

J.P. MorganSVB LeerinkPiper SandlerBMO Capital Markets

December , 2020
