PTC THERAPEUTICS, INC.
Form 424B5
January 22, 2019

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Filed Pursuant to Rule 424(b)(5)
Registration No. 333-220151

The information in this preliminary prospectus supplement is not complete and may be changed. A registration statement relating to these securities has been filed with the Securities and Exchange Commission and is effective. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell these securities and they are not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to Completion, Dated January 22, 2019

Prospectus Supplement
(To Prospectus Dated August 24, 2017)

$200 million

Common Stock

PTC Therapeutics, Inc. is offering $200 million of shares of our common stock, par value $0.001 per share. The public offering price is $ per share.

Our common stock trades on The Nasdaq Global Select Market, or the Nasdaq, under the trading symbol "PTCT". On January 18, 2019, the last sale price of our common stock as reported on the Nasdaq was $34.44 per share.

Investing in our common stock involves risks. See "Risk Factors" beginning on page S-6 of this prospectus supplement.

	Per Share	Total
Public offering price	$	$
Underwriting discounts and commissions	$	$
Proceeds, before expenses, to us	$	$

We have granted the underwriter an option for a period of 30 days from the date of this prospectus supplement to purchase up to an additional $30 million of shares of our common stock at the public offering price, less the underwriting discounts and commissions.

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

The underwriter expects to deliver the shares to the investors on or about January , 2019.

RBC Capital Markets

January , 2019

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ABOUT THIS PROSPECTUS SUPPLEMENT

This document is in two parts. The first part is this prospectus supplement, which describes the specific terms of this offering and also adds to and updates information contained in the accompanying prospectus and the documents incorporated by reference herein and therein. The second part, the accompanying prospectus, 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 herein or 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 underwriter has not authorized anyone to provide any information other than that contained or incorporated by reference in this prospectus supplement, in the accompanying prospectus or in any free writing prospectus prepared by or on behalf of us or to which we have referred you. We and the underwriter 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. You should assume that the information appearing in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein and in any free writing prospectus that we have authorized for use in connection with this offering is accurate only as of the date of those respective documents. It is important for you to read and consider all information contained in this prospectus supplement and in the accompanying prospectus, 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 by Reference" in this prospectus supplement and in the accompanying prospectus.

Other than in the United States, no action has been taken by us or the underwriter 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

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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.

Unless the context otherwise indicates, references in this prospectus to "PTC," "we," "our," "us" and "the Company" refer, collectively, to PTC Therapeutics, Inc., a Delaware corporation, and its consolidated subsidiaries.

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SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the information incorporated by reference herein and therein include "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, or the Exchange Act, that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained or incorporated by reference in this prospectus supplement or the accompanying prospectus, including statements regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "might," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

The forward-looking statements in this prospectus, the accompanying prospectus and the information incorporated by reference herein and therein include, among other things, statements about:

our ability to realize the anticipated benefits of our acquisition of Agilis Biotherapeutics, Inc., or Agilis, including the possibility that the expected impact of benefits from the acquisition, including with respect to the business of Agilis and our expectations with respect to the potential achievement of development, regulatory and sales milestones and our contingent payments to the former Agilis equityholders with respect thereto, will not be realized or will not be realized within the expected time period, significant transaction costs, the integration of Agilis's operations and employees into our business, our ability to obtain marketing approval of our gene therapy for the treatment of Aromatic L-Amino Acid Decarboxylase, or AADC, deficiency, or PTC-AADC, and other product candidates we acquired from Agilis, unknown liabilities, the risk of litigation and/or regulatory actions related to the acquisition, and other business effects, including the effects of industry, market, economic, political or regulatory conditions;

our ability to negotiate, secure and maintain adequate pricing, coverage and reimbursement terms and processes on a timely basis, or at all, with third-party payors for Emflaza (deflazacort) for the treatment of Duchenne muscular dystrophy, or DMD, in the United States and for Translarna (ataluren) for the treatment of nonsense mutation DMD, or nmDMD, in the European Economic Area, or EEA, and other countries in which we have or may obtain regulatory approval, or in which there exist significant reimbursed early access programs, or EAP programs;

our ability to maintain our marketing authorization of Translarna for the treatment of nmDMD in the EEA (which is subject to the specific obligation to conduct and submit the results of Study 041 to the European Medicines Agency, or EMA, and annual review and renewal by the European Commission following reassessment of the benefit-risk balance of the authorization by the EMA);

our ability to enroll, fund, and complete Study 041, a multicenter, randomized, double-blind, 18-month, placebo-controlled clinical trial of Translarna for the treatment of

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nmDMD followed by an 18-month open label extension, according to the protocol agreed with the EMA, and by the trial's deadline;

the anticipated period of market exclusivity for Emflaza for the treatment of DMD in the United States under the Orphan Drug Act of 1983, or the Orphan Drug Act, the Drug Price Competition and Patent Term Restoration Act of 1984, or the Hatch-Waxman Act;

our expectations with respect to our acquisition of all rights to Emflaza from Marathon Pharmaceuticals, LLC (now known as Complete Pharma Holdings, LLC), or Marathon, including with respect to our ability to realize the anticipated benefits of the acquisition (including with respect to future revenue generation and contingent payments to Marathon based on annual net sales);

our ability to complete any dystrophin study necessary in order to resolve the matters set forth in the FDA's denial of our appeal to the Complete Response Letter we received from the FDA in connection with our New Drug Application, or NDA, for Translarna for the treatment of nmDMD, and our ability to perform additional clinical trials, non-clinical studies or CMC assessments or analyses at significant cost;

the timing and scope of our continued commercialization of Translarna as a treatment for nmDMD in the EEA or other territories outside of the United States;

our ability to obtain additional and maintain existing reimbursed named patient and cohort EAP programs for Translarna for the treatment of nmDMD on adequate terms, or at all;

our expectations and the potential financial impact and benefits related to our Collaboration and Licensing Agreement with Akcea Therapeutics, Inc., or Akcea, including with respect to the timing of regulatory approval of Tegsedi™ (inotersen) and Waylivra™ (volanesorsen) in countries in which we are licensed to commercialize them, the potential commercialization of Tegsedi and Waylivra, and our expectations with respect to contingent payments to Akcea based on the potential achievement of certain regulatory milestones and royalty payments by us to Akcea based on our potential achievement of certain net sales thresholds;

our estimates regarding the potential market opportunity for Translarna, Emflaza, PTC-AADC, Tegsedi, Waylivra, Risdiplam or any other product candidate, including the size of eligible patient populations and our ability to identify such patients;

our estimates regarding expenses, future revenues, third-party discounts and rebates, capital requirements and needs for additional financing, including our ability to maintain the level of our expenses consistent with our internal budgets and forecasts and to secure additional funds on favorable terms or at all;

the timing and conduct of our ongoing, planned and potential future clinical trials and studies of Translarna for the treatment of nmDMD, aniridia, and Dravet syndrome/CDKL5, each caused by nonsense mutations, as well as our studies in spinal muscular atrophy and our oncology program, including the timing of initiation, enrollment and completion of the trials and the period during which the results of the trials will become available;

the rate and degree of market acceptance and clinical utility of Translarna, Emflaza, PTC-AADC, Tegsedi, Waylivra and Risdiplam;

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the ability and willingness of patients and healthcare professionals to access Translarna through alternative means if pricing and reimbursement negotiations in the applicable territory do not have a positive outcome;

the timing of, and our ability to obtain additional marketing authorizations for, Translarna and our other product candidates;

the ability of Translarna, Emflaza, PTC-AADC, Tegsedi, Waylivra and Risdiplam and our other product candidates to meet existing or future regulatory standards;

our ability to maintain the current labeling under the marketing authorization in the EEA or expand the approved product label of Translarna for the treatment of nmDMD in non-ambulatory patients or otherwise;

the potential receipt of revenues from future sales of Translarna, Emflaza and other product candidates, including our ability to earn a profit from sales or licenses of Translarna for the treatment of nmDMD in the countries in which we have or may obtain regulatory approval and of Emflaza for the treatment of DMD in the United States;

the potential impact that enrollment, funding and completion of Study 041 may have on our revenue growth;

our sales, marketing and distribution capabilities and strategy, including the ability of our third-party manufacturers to manufacture and deliver Translarna and Emflaza and any other product candidate in clinically and commercially sufficient quantities and the ability of distributors to process orders in a timely manner and satisfy their other obligations to us;

our ability to establish and maintain arrangements for the manufacture of Translarna, Emflaza and our other product candidates that are sufficient to meet clinical trial and commercial launch requirements;

our ability to satisfy our obligations under the terms of the credit and security agreement with MidCap Financial Trust, or MidCap Financial, as administrative agent and MidCap Financial and certain other financial institutions as lenders thereunder;

our other regulatory submissions, including with respect to timing and outcome of regulatory review;

our plans to pursue development of Translarna for additional indications;

our ability to advance our earlier stage programs, including our oncology program;

our plans to pursue research and development of other product candidates;

whether we may pursue business development opportunities, including potential collaborations, alliances, and acquisition or licensing of assets and our ability to successfully develop or commercialize any assets to which we may gain rights pursuant to such business development opportunities;

the potential advantages of Translarna, Emflaza, PTC-AADC, Tegsedi, Waylivra and Ridisplam and any other product candidate;

our intellectual property position;

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- the impact of government laws and regulations;
- the impact of litigation that has or may be brought against us or of litigation that we are pursuing against others;
- our competitive position;
- our expectations with respect to the development and regulatory status of our product candidates, including Risdiplam, and program directed against spinal muscular atrophy in collaboration with F. Hoffmann La Roche Ltd and Hoffmann La Roche Inc., which we refer to collectively as Roche, and the Spinal Muscular Atrophy Foundation, or the SMA Foundation, and our estimates regarding future revenues from achievement of milestones in that program;
- our preliminary financial results for the 2018 fiscal year, including expected net product revenue and cash and cash equivalents; and
- our expected use of proceeds from this offering.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. We have included important factors in the cautionary statements included in this prospectus supplement, the accompanying prospectus and the information incorporated by reference herein and therein, particularly in the "Risk Factors" section of this prospectus supplement, in the "Risk Factors" sections of our Annual Report on Form 10-K for the year ended December 31, 2017 and our Quarterly Reports on Form 10-Q for the fiscal quarters ended March 31, 2018, June 30, 2018 and September 30, 2018, and in Exhibit 99.2 to our Current Report on Form 8-K filed on August 24, 2018, that we believe could cause actual results or events to differ materially from the forward-looking statements that we make. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make. We do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by law.

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PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights selected information contained elsewhere in this prospectus supplement and the accompanying prospectus and in the documents we incorporate by reference. This summary does not contain all of the information you should consider before making an investment decision. You should read this entire prospectus supplement and the accompanying prospectus carefully, especially the risks of investing in our common stock discussed under "Risk Factors" beginning on page S-6 of this prospectus supplement, in the "Risk Factors" sections of our Annual Report on Form 10-K for the year ended December 31, 2017 and our Quarterly Reports on Form 10-Q for the fiscal quarters ended March 31, 2018, June 30, 2018 and September 30, 2018, and in Exhibit 99.2 to our Current Report on Form 8-K filed on August 24, 2018, along with our consolidated financial statements and notes to those consolidated financial statements and the other information incorporated by reference in this prospectus supplement and the accompanying prospectus.

PTC Therapeutics, Inc.

We are a science-led global biopharmaceutical company focused on the discovery, development and commercialization of clinically-differentiated medicines that provide benefits to patients with rare disorders. Our ability to globally commercialize products is the foundation that drives our continued investment in a robust pipeline of transformative medicines and our mission to provide access to best-in-class treatments for patients who have an unmet medical need. Our strategy is to bring best-in-class therapies with differentiated clinical benefit to patients affected by rare disorders and to leverage our global commercial infrastructure to maximize value for our patients and other stakeholders.

Global DMD Franchise

We have two products, Translarna (ataluren) and Emflaza (deflazacort), for the treatment of Duchenne muscular dystrophy, or DMD, a rare, life threatening disorder. Translarna received marketing authorization from the European Commission in August 2014 for the treatment of nonsense mutation DMD, or nmDMD, in ambulatory patients aged five years and older in the 31 member states of the European Economic Area, or EEA. In July 2018, the European Commission renewed our marketing authorization and approved a label-extension to our marketing authorization to include patients from two to five years of age. The marketing authorization is subject to annual review and renewal by the European Commission following reassessment by the European Medicines Agency, or EMA, of the benefit-risk balance of continued authorization, as well as our satisfaction of any specific obligation or other requirement placed upon the marketing authorization, including Study 041, a three-year clinical trial to confirm the efficacy and safety of Translarna in the approved patient population. During the quarter ended September 30, 2018, we recognized $30.4 million in net sales of Translarna. Translarna is currently available for the treatment of nmDMD in over 25 countries on a commercial basis or through a reimbursed early access program, or EAP program. We hold worldwide commercialization rights to Translarna for all indications in all territories. We acquired all rights to Emflaza from Marathon Pharmaceuticals, LLC (now known as Complete Pharma Holdings, LLC), or Marathon, in April 2017, and we began commercialization of Emflaza in the United States in May 2017. Emflaza is

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approved in the United States for the treatment of DMD in patients five years and older. During the quarter ended September 30, 2018, Emflaza achieved net sales of $22.6 million.

Agilis Transaction

On August 23, 2018, we acquired Agilis Biotherapeutics, Inc., or Agilis, which prior to the acquisition was a privately-held biotechnology company advancing an innovative gene therapy platform for rare monogenic diseases that affect the central nervous system, or CNS. With the acquisition of Agilis, we now have a pipeline of gene therapy product candidates, including PTC-AADC for the treatment of Aromatic L-Amino Acid Decarboxylase, or AADC, deficiency, or AADC deficiency, a rare CNS disorder arising from reductions in the enzyme AADC that result from mutations in the dopa decarboxylase gene. We are preparing a biologics license application, or BLA, for PTC-AADC for the treatment of AADC deficiency in the United States, which we anticipate submitting to the U.S. Food and Drug Administration, or FDA, in the second half of 2019. We are also preparing a marketing authorization application, or MAA, for PTC-AADC for the treatment of AADC deficiency in the European Union, or EU.

Akcea Partnership

We hold the rights for the commercialization of Tegsedi (inotersen) and Waylivra (volanesorsen) for the treatment of rare diseases in countries in Latin America and the Caribbean pursuant to our collaboration and license Agreement with Akcea Therapeutics, Inc. Tegsedi has received marketing authorization in the United States, EU and Canada for the treatment of stage 1 or stage 2 polyneuropathy in adult patients with hereditary transthyretin amyloidosis, or hATTR amyloidosis, and was recently granted priority review by ANVISA, the Brazilian Health Regulatory Authority. Waylivra is currently under regulatory review in the EU for the treatment of familial chylomicronemia syndrome, or FCS.

The Splicing Franchise

We also have a spinal muscular atrophy, or SMA, collaboration with F. Hoffman-La Roche Ltd and Hoffman-La Roche Inc., which we refer to collectively as Roche, and the Spinal Muscular Atrophy Foundation, or SMA Foundation. Currently, our collaboration has two pivotal clinical trials ongoing to evaluate the safety and effectiveness of Risdiplam (RG7916, RO7034067), the lead compound in the SMA program. Roche is preparing an NDA and a MAA for Risdiplam for the treatment of SMA in the United States and the EU, respectively, which Roche anticipates submitting to the FDA and the EMA in the second half of 2019. In addition, we have a pipeline of product candidates that are in early clinical and pre-clinical development, including PTC258, our product candidate for the treatment of Familial dysautonomia, a rare genetic neurological disorder that affects the sensory and autonomic nervous systems, causing life-threatening medical complications from birth. We expect to begin IND-enabling studies for PTC258 in late 2019. Our pre-clinical and discovery programs are focused on the development of new treatments for multiple therapeutic areas, including rare diseases and oncology.

Recent Developments

We are currently in the process of finalizing our financial results for the 2018 fiscal year. Based on preliminary unaudited information and management estimates for the 2018 fiscal year,

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and subject to the completion of our financial closing procedures, on January 7, 2018, we announced certain preliminary financial results for the 2018 fiscal year, including that we expect Translarna net product revenue for the treatment of nmDMD of approximately $171 million for the 2018 fiscal year, an increase of 18% from the 2017 fiscal year; Emflaza net product revenue for the treatment of DMD of approximately $91 million for the 2018 fiscal year, an increase from $28.8 million for the 2017 fiscal year; and approximately $227 million in year-end cash and cash equivalents for the 2018 fiscal year.

We have provided approximate values for our preliminary results because our financial closing procedures for the 2018 fiscal year are not yet complete. The above information was not prepared with a view toward complying with the guidelines established by the American Institute of Certified Public Accountants with respect to projected financial information, but, in the view of our management, was prepared on a reasonable basis, reflects the best currently available estimates and judgments, and presents, to the best of management's knowledge and belief, our expectations for the 2018 fiscal year. Neither our independent auditors, nor any other independent accountants, have compiled, examined, or performed any procedures with respect to the above information, nor have they expressed any opinion or any other form of assurance on such information, and assume no responsibility for, and disclaim any association with, the above information. In addition, the foregoing information is subject to revision as we complete our financial closing procedures for the 2018 fiscal year. Actual results for the 2018 fiscal year may differ materially from the above information as a result of, among other things, the important factors discussed under "Risk Factors" and elsewhere in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference herein and therein. We disclaim any obligation to update these forward-looking statements.

The above information should not be viewed as a substitute for full financial statements prepared in accordance with generally accepted accounting principles. In addition, the above information is not necessarily indicative of the results to be achieved for any future period and is subject to risks and uncertainties, many of which are not within our control. The above information should be read together with our consolidated financial statements and notes to those consolidated financial statements and the other information incorporated by reference in this prospectus supplement and the accompanying prospectus.

Company Information

We were incorporated under the laws of the State of Delaware on March 31, 1998, under the name PTC Therapeutics, Inc. Our principal executive offices are located at 100 Corporate Court, South Plainfield, New Jersey 07080. Our telephone number is (908) 222-7000. We maintain a website at *www.ptcbio.com*. The information contained on, or that can be accessed through, our website is not a part of this prospectus supplement or the accompanying prospectus. We have included our website address in this prospectus supplement and the accompanying prospectus solely as an inactive textual reference.

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The Offering

Common Stock Offered by Us	$200 million of shares
Common Stock to Be Outstanding After This Offering	56,413,347 shares (or 57,284,428 shares if the underwriter exercises in full its option to purchase additional shares) based upon an offering of $200 million at an assumed public offering price of $34.44 per share (the last reported sale price of our common stock on the Nasdaq on January 18, 2019).
Option to Purchase Additional Shares Offered to the Underwriter	The underwriter has an option to purchase up to an additional $30 million of shares of our common stock. The underwriter can exercise this option at any time within 30 days from the date of this prospectus supplement.
Use of Proceeds	We estimate that the net proceeds from this offering, after deducting underwriting discounts and commissions and estimated offering expenses payable by us, will be approximately $ million (or approximately $ million if the underwriter exercises in full its option to purchase additional shares), based on the public offering price of $ per share. We intend to use the net proceeds from this offering to fund our research and development efforts, our efforts to increase our manufacturing capabilities for our gene therapy platform and our commercialization activities, and for working capital and other general corporate purposes. General corporate purposes may include other research and development expenditures, repayment and refinancing of debt, other capital expenditures and further strategic transactions to expand and diversify our product pipeline, including through the acquisition of assets, businesses, rights to products, product candidates or technologies or through strategic alliances or collaborations. See "Use of Proceeds" for more information.
Risk Factors	You should read the "Risk Factors" section of this prospectus supplement for a discussion of factors to consider carefully before deciding to purchase shares of our common stock.
Nasdaq Global Select Market Symbol	PTCT

The number of shares of our common stock to be outstanding after this offering is based on 50,606,147 shares of our common stock outstanding as of December 31, 2018.

The number of shares of our common stock to be outstanding after this offering excludes:

- 8,556,358 shares of our common stock issuable upon the exercise of outstanding stock options as of December 31, 2018, at a weighted-average exercise price of $28.56 per share;

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459,413 shares of our common stock issuable upon the vesting of outstanding restricted stock units as of December 31, 2018;

112,066 shares of our common stock issuable upon the vesting of outstanding restricted stock awards as of December 31, 2018;

697,708 additional shares of our common stock reserved for future issuance under our 2013 Long Term Incentive Plan as of December 31, 2018;

591,048 shares of our common stock reserved for future issuance under our Employee Stock Purchase Plan as of December 31, 2018;

7,160 shares of our common stock issuable upon the exercise of warrants outstanding as of December 31, 2018, at a weighted-average exercise price of $171.43 per share; and

the shares of our common stock reserved for issuance upon conversion of our 3.00% convertible senior notes due August 12, 2022.

As of January 1, 2019, an additional 2,024,932 shares of our common stock were added to and became available for future issuance under our 2013 Long Term Incentive Plan pursuant to such plan's annual evergreen provision. On January 22, 2019, we approved grants to our employees and directors of stock options for a total of 2,178,916 shares of our common stock at an exercise price per share equal to the closing price per share on the Nasdaq on January 22, 2019, restricted stock units for a total of 268,426 shares of our common stock and restricted stock awards for a total of 34,173 shares of our common stock as part of our regular annual compensation cycle pursuant to our 2013 Long Term Incentive Plan, and of stock options for 170,050 shares of our common stock to new hire employees as inducement grants pursuant to Nasdaq rules. The shares of common stock described in this paragraph are also excluded from the number of shares of our common stock outstanding as of December 31, 2018 and to be outstanding after this offering.

Except as otherwise noted, we have presented the information in this prospectus supplement assuming:

no exercise by the underwriter in this offering of the option to purchase up to an additional $30 million of shares of our common stock in this offering;

no exercise of outstanding stock options or warrants; and

no conversion of our 3.00% convertible senior notes.

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RISK FACTORS

Investing in our common stock involves significant risks. In deciding whether to invest, and in consultation with your own financial and legal advisors, you should carefully consider the following risk factors and the risks described in the "Risk Factors" sections of our Annual Report on Form 10-K for the year ended December 31, 2017 and our Quarterly Reports on Form 10-Q for the fiscal quarters ended March 31, 2018, June 30, 2018 and September 30, 2018, and in Exhibit 99.2 to our Current Report on Form 8-K filed on August 24, 2018, as well as the other information contained in this prospectus supplement, the accompanying prospectus and in our filings with the Securities and Exchange Commission, or the SEC, that we have incorporated by reference in this prospectus supplement and the accompanying prospectus. Any of these risks could have a material adverse effect on our business, financial condition, results of operations and prospects and cause the value of our stock to decline, which could cause you to lose all or part of your investment. The risks and uncertainties we have described are not the only ones facing our company. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also affect our business operations.

Risks Related to this Offering

Our management may invest or spend the proceeds of this offering in ways with which you may not agree or in ways which may not yield a significant return, if any.

Our management will have broad discretion over the use of the net proceeds from this offering and could use them for purposes other than those contemplated at the time of this offering. You may not agree with the manner in which our management chooses to allocate and spend these net proceeds. You will not have the opportunity, as part of your investment decision, to assess whether the proceeds are being used appropriately. The net proceeds may be used for corporate purposes that do not increase our operating results or market value. Until the net proceeds are used, they may be placed in investments that do not produce significant income or investments that lose value.

You will suffer immediate dilution of your investment.

The public offering price of our common stock will be substantially higher than the net tangible book value per share of our common stock. Therefore, if you purchase shares of our common stock in this offering, you will pay a price per share that substantially exceeds our net tangible book value per share after this offering. To the extent outstanding options or warrants are exercised or shares of our common stock are issued upon the vesting of restricted stock units or upon the conversion of our 3.00% convertible senior notes due August 12, 2022, you will incur further dilution. Based on the public offering price of $ per share, you will experience immediate dilution of $ per share, representing the difference between our as adjusted net tangible book value per share after giving effect to this offering at the public offering price. See "Dilution."

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

In order to raise additional capital, we may in the future offer additional shares of our common stock or other securities convertible into or exchangeable for our common stock at prices

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

Because we do not anticipate paying any cash dividends on our capital in the foreseeable future, capital appreciation, if any, will be our stockholders' sole source of gain.

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the development and growth of our business. In addition, the terms of our existing credit and security agreement with MidCap Financial Trust preclude us, and the terms of any future debt agreements may preclude us, from paying dividends without lender consent. As a result, capital appreciation, if any, of our common stock will be our stockholders' sole source of gain for the foreseeable future.

Future sales of shares of our common stock, including by us or our directors and executive officers, could cause the market price of our common stock to drop significantly, even if our business is doing well.

A substantial portion of our outstanding common stock is freely tradeable. Some of these shares are currently "restricted" securities as a result of securities laws, but are able to be sold, subject to any applicable volume limitations under federal securities laws with respect to affiliate sales. As such, sales of a substantial number of shares of our common stock in the public market could occur at any time. These sales, or the perception in the market that the holders of a large number of shares intend to sell shares, by us or others, could reduce the market price of our common stock.

We have issued a significant number of equity awards under our equity compensation plans or as inducement grants to new hire employees pursuant to Nasdaq rules. The shares underlying these awards are or, with respect to certain option grants, have been or will be registered on a Form S-8 registration statement. As a result, upon vesting these shares can be freely exercised and sold in the public market upon issuance, subject to volume limitations applicable to affiliates. The exercise of options or warrants and the subsequent sale of the underlying common stock or the sale of restricted stock upon vesting could cause a decline in our stock price. These sales also might make it difficult for us to sell equity securities in the future at a time and at a price that we deem appropriate.

Certain of our employees, executive officers and directors have entered or may enter into Rule 10b5-1 plans providing for sales of shares of our common stock from time to time. Under a Rule 10b5-1 plan, a broker executes trades pursuant to parameters established by the employee, director or officer when entering into the plan, without further direction from the employee, officer or director. A Rule 10b5-1 plan may be amended or terminated in some circumstances. Our employees, executive officers and directors may also buy or sell additional shares outside of a Rule 10b5-1 plan when they are not in possession of material, nonpublic information. As of December 31, 2018, an aggregate of 708,190 shares of our common stock, including shares of our

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common stock underlying stock option awards, held by our executive officers was subject to a Rule 10b5-1 plan.

In connection with our acquisition of Emflaza, we issued an affiliate of Marathon 6,683,598 shares of our common stock. These shares are able to be freely sold in the public market subject to any requirements and restrictions, including any applicable volume limitations, imposed by Rule 144 under the Securities Act. In addition, in connection with our acquisition of Agilis Biotherapeutics, Inc., or Agilis, we issued Agilis equityholders 3,500,907 shares of our common stock, which shares are able to be freely sold in the public market pursuant to a resale registration statement on Form S-3 that we filed with the SEC. The sale or resale of these shares in the public market, or the market's expectation of such sales, may result in an immediate and substantial decline in our stock price. Such a decline will adversely affect our investors and also might make it difficult for us to sell equity securities in the future at a time and at a price that we deem appropriate.

After this offering, we will have outstanding 56,413,347 shares of our common stock, based on 50,606,147 shares of our common stock outstanding as of December 31, 2018 and an assumed public offering price of $34.44 per share, the last reported sale price of our common stock on the Nasdaq on January 18, 2019. In addition, we have a significant number of shares that are subject to outstanding options and warrants. The exercise of these options and warrants and the subsequent sale of the underlying common stock could cause a further decline in our stock price. These sales also might make it difficult for us to sell equity securities in the future at a time and at a price that we deem appropriate.

In connection with this offering, we have entered into a lock-up agreement for a period of 60 days following this offering. In addition, our directors and executive officers have entered into lock-up agreements for a period of 60 days following this offering, which cover 1,608,314 shares of our outstanding common stock (excluding shares underlying stock option awards). The remaining 48,997,833 shares outstanding as of December 31, 2018 are not subject to a lock-up agreement, but affiliate sales may be subject to restrictions under federal securities laws. We and our directors and executive officers may be released from lock-up prior to the expiration of the lock-up period at the sole discretion of RBC Capital Markets, LLC. Upon expiration or earlier release of the lock-up agreements described in the "Underwriting" section of this prospectus supplement and the accompanying prospectus, we and our directors and executive officers may sell securities into the market, which could adversely affect the market price of shares of our common stock. In addition, during the lock-up period and thereafter, sales of shares of common stock held by our directors and executive officers are permitted under trading plans, as in effect as of the date of the applicable lock-up agreement, established pursuant to Rule 10b5-1 of the Exchange Act and in certain other limited exceptions. We cannot predict the size of future issuances or the effect, if any, that this offering or any future issuances may have on the market price for our common stock.

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USE OF PROCEEDS

We estimate that the net proceeds we will receive from this offering will be approximately $ million, after deducting underwriting discounts and commissions and estimated offering expenses payable by us and based on the public offering price of $ per share. If the underwriter exercises in full its option to purchase additional shares, we estimate that the net proceeds to us will be approximately $ million, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

We intend to use the net proceeds from this offering to fund our research and development efforts, including clinical trials and studies with respect to our products and product candidates and potential additional indications, including our programs for our gene therapy platform and for alternative splicing for the treatment of rare disorders and oncology, our efforts to increase our manufacturing capabilities for our gene therapy platform and our commercialization activities for Translarna for the treatment of nmDMD outside of the United States, for Emflaza for the treatment of DMD in the United States, and for Tegsedi and Waylivra for the treatment of rare diseases in countries in Latin America and the Caribbean, and for working capital and other general corporate purposes. General corporate purposes may include research and development expenditures, repayment and refinancing of debt, capital expenditures and further strategic transactions to expand and diversify our product pipeline, including through the acquisition of assets, businesses, rights to products, product candidates or technologies or through strategic alliances or collaborations. We have not determined the amount of net proceeds to be used specifically for such purposes. As a result, management will retain broad discretion over the allocation of the net proceeds.

This expected use of 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 may vary significantly depending on numerous factors, including the progress of our development and commercialization efforts, the status of and results from clinical trials and studies, the timing of regulatory submissions and the outcome of regulatory reviews, as well as any collaborations that we may enter into with third parties for our product candidates, and any unforeseen cash needs. We have no current agreements or commitments for any material acquisition of assets, businesses, rights to products, product candidates or technologies or any material strategic alliances or collaborations.

Based on our current operating plans, we estimate that the net proceeds from this offering, together with our existing cash, cash equivalents and marketable securities, our anticipated cashflows from product sales and research funding that we expect to receive under our collaborations, will be sufficient to fund our operating expenses and capital expenditure requirements for at least the next twelve months. We have based this estimate on assumptions that may prove to be wrong, and we could use our capital resources sooner than we currently expect. This estimate does not reflect any additional expenditures that may result from any further strategic transactions to expand and diversify our product pipeline, including acquisitions of assets, businesses, rights to products, product candidates or technologies or strategic alliances or collaborations that we may pursue.

Pending our use of the net proceeds from this offering, we intend to invest the net proceeds in a variety of capital preservation investments, including short-term, investment grade, interest bearing instruments and U.S. government securities.

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DIVIDEND POLICY

We have never declared or paid cash dividends on our common stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. We do not intend to pay cash dividends to holders of our common stock in the foreseeable future. In addition, the terms of our existing credit and security agreement with MidCap Financial Trust preclude us from paying cash dividends without MidCap Financial Trust's consent.

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CAPITALIZATION

The following table sets forth our cash, cash equivalents, marketable securities and long-term debt and our capitalization as of September 30, 2018:

- on an actual basis; and
- on an as adjusted basis to give effect to our issuance and sale of shares of our common stock in this offering at the public offering price of $ per share, and our receipt of net proceeds therefrom, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

You should read this table together with our consolidated financial statements and condensed consolidated financial statements and related notes incorporated by reference in this prospectus supplement and the accompanying prospectus.

	As of September 30, 2018	
	Actual	As Adjusted
(Unaudited, in thousands, except par value data)		
Cash and cash equivalents	$ 206,913	$
Marketable securities	42,491	42,491
Long-term debt	144,258	144,258
Stockholders' deficit:		
Preferred stock, $0.001 par value per share, undesignated 5,000,000 shares, no shares issued or outstanding, actual or as adjusted		
Common stock, $0.001 par value per share, authorized 125,000,000 shares, issued and outstanding 50,432,655 shares actual, issued and outstanding shares as adjusted	51	
Additional paid-in capital	1,275,004	
Accumulated other comprehensive income	1,628	1,628
Accumulated deficit	(890,593)	(890,593)
Total stockholders' equity	386,090	
Total capitalization	$ 530,348	$

The table above is based on actual shares of our common stock outstanding as of September 30, 2018 and excludes as of such date:

- 8,521,232 shares of our common stock issuable upon the exercise of outstanding stock options at a weighted-average exercise price of $28.44 per share;
- 467,781 shares of our common stock issuable upon the vesting of outstanding restricted stock units;
- 112,566 shares of our common stock issuable upon the vesting of outstanding restricted stock awards;
- 665,194 additional shares of our common stock reserved for future issuance under our 2013 Long Term Incentive Plan;

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642,712 shares of our common stock reserved for future issuance under our Employee Stock Purchase Plan;

7,160 shares of our common stock issuable upon the exercise of outstanding warrants at a weighted-average exercise price of $171.43 per share; and

the shares of our common stock reserved for issuance upon conversion of our 3.00% convertible senior notes due August 12, 2022.

As of January 1, 2019, an additional 2,024,932 shares of our common stock were added to and became available for future issuance under our 2013 Long Term Incentive Plan pursuant to such plan's annual evergreen provision. On January 22, 2019, we approved grants to our employees and directors of stock options for a total of 2,178,916 shares of our common stock at an exercise price per share equal to the closing price per share on the Nasdaq on January 22, 2019, restricted stock units for a total of 268,426 shares of our common stock and restricted stock awards for a total of 34,173 shares of our common stock as part of our regular annual compensation cycle pursuant to our 2013 Long Term Incentive Plan, and of stock options for 170,050 shares of our common stock to new hire employees as inducement grants pursuant to Nasdaq rules. The shares of common stock described in this paragraph are also excluded from the number of shares of our common stock outstanding as of September 30, 2018 and to be outstanding after this offering.

The as adjusted information discussed above will be based on the actual offering price and other terms of this offering determined at pricing.

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DILUTION

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

Our historical net tangible book value as of September 30, 2018 was $386.1 million, or $7.66 per share of our common stock. Historical net tangible book value per share represents the amount of our total tangible assets less total liabilities, divided by the number of shares of our common stock outstanding. After giving effect to our issuance and sale of shares of our common stock in this offering at the public offering price of $ per share, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our net tangible book value as of September 30, 2018 would have been $ million, or $ per share. This represents an immediate increase in net tangible book value per share of $ to existing stockholders and immediate dilution of $ in net tangible book value per share to new investors purchasing common stock in this offering. Dilution per share to new investors is determined by subtracting net tangible book value per share after this offering from the public offering price per share paid by new investors. The following table illustrates this dilution on a per share basis:

Public offering price per share		$
Historical net tangible book value per share as of September 30, 2018	$ 7.66	
Increase in net tangible book value per share attributable to shares of common stock to be issued in this offering	$	
As adjusted net tangible book value per share after this offering		$
Dilution per share to new investors		$

The foregoing table and calculations are based on actual shares of our common stock outstanding as of September 30, 2018 and exclude as of such date:

- 8,521,232 shares of our common stock issuable upon the exercise of outstanding stock options at a weighted-average exercise price of $28.44 per share;
- 467,781 shares of our common stock issuable upon the vesting of outstanding restricted stock units;
- 112,566 shares of our common stock issuable upon the vesting of outstanding restricted stock awards;
- 665,194 additional shares of our common stock reserved for future issuance under our 2013 Long Term Incentive Plan;
- 642,712 shares of our common stock reserved for future issuance under our Employee Stock Purchase Plan;

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7,160 shares of our common stock issuable upon the exercise of outstanding warrants at a weighted-average exercise price of $171.43 per share; and

the shares of our common stock reserved for issuance upon conversion of our 3.00% convertible senior notes due August 12, 2022.

As of January 1, 2019, an additional 2,024,932 shares of our common stock were added to and became available for future issuance under our 2013 Long Term Incentive Plan pursuant to such plan's annual evergreen provision. On January 22, 2019, we approved grants to our employees and directors of stock options for a total of 2,178,916 shares of our common stock at an exercise price per share equal to the closing price per share on the Nasdaq on January 22, 2019, restricted stock units for a total of 268,426 shares of our common stock and restricted stock awards for a total of 34,173 shares of our common stock as part of our regular annual compensation cycle pursuant to our 2013 Long Term Incentive Plan, and of stock options for 170,050 shares of our common stock to new hire employees as inducement grants pursuant to Nasdaq rules. The shares of common stock described in this paragraph are also excluded from the number of shares of our common stock outstanding as of September 30, 2018 and to be outstanding after this offering.

If the underwriter exercises its option to purchase additional shares of our common stock or if any additional shares are issued in connection with outstanding options or warrants, there will be further dilution to new investors.

The as adjusted information discussed above will be based on the actual offering price and other terms of this offering determined at pricing.

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UNDERWRITING

We are offering the shares of our common stock described in this prospectus through an underwriter, RBC Capital Markets, LLC. We have entered into an underwriting agreement with the underwriter. Subject to the terms and conditions of the underwriting agreement, we have agreed to sell to the underwriter, and the underwriter has 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 our common stock listed in the following table:

	Number of Shares
RBC Capital Markets, LLC	
Total	

The underwriter is committed to purchase all the shares of our common stock offered by us if it purchases any shares.

The underwriter proposes to offer the shares of our common stock directly to the public at the public offering price set forth on the cover page of this prospectus supplement and to certain dealers at that price less a concession not in excess of $ per share. After the public offering of the shares, the offering price and the selling concession may be changed by the underwriter. Sales of shares made outside of the United States may be made by affiliates of the underwriter.

The underwriter has an option to buy up to $30 million of shares of our common stock from us. The underwriter has 30 days from the date of this prospectus to exercise this option. If any additional shares of our common stock are purchased, the underwriter 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 underwriter assuming both no exercise and full exercise of the underwriter's option.

	Without option exercise	With full option exercise
Per Share	$	$
Total	$	$

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 $650,000.

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

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We have agreed that we will not (1) offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase or otherwise transfer or dispose of, directly or indirectly, or file with the Securities and Exchange Commission a registration statement under the Securities Act relating to, any shares of our common stock or securities convertible into or exchangeable or exercisable for any shares of our common stock, or publicly disclose the intention to make any offer, sale, pledge, disposition or filing, or (2) enter into any swap or other arrangement that transfers all or a portion of the economic consequences associated with the ownership of any shares of our common stock or any such other securities (regardless of whether any of these transactions are to be settled by the delivery of shares of our common stock or such other securities, in cash or otherwise), in each case without the prior written consent of RBC Capital Markets, LLC for a period of 60 days after the date of this prospectus, other than (A) the shares of our common stock to be sold pursuant to the underwriting agreement, (B) any shares of our common stock issued upon the exercise of options or warrants, restricted stock units or restricted stock awards, or upon the vesting of equity awards, including restricted stock units and restricted stock awards, granted under our existing management incentive plans and shares of our common stock issued pursuant to our employee stock purchase plan, or warrants described as outstanding in this prospectus, (C) any options, restricted stock units, restricted stock awards, and other equity awards granted under our existing management incentive plans, including our employee stock purchase plan, (D) our filing of a registration statement on Form S-8 or a successor form thereto, (E) any shares of our common stock, options and equity awards granted to new employees as inducement awards pursuant to Nasdaq Listing Rule 5635(c)(4) and (F) any shares of our common stock or other securities issued in connection with a transaction that includes a commercial relationship (including joint ventures, marketing or distribution arrangements, collaboration agreements or intellectual property license agreements) or any acquisition of assets or not less than a majority or controlling portion of the equity of another entity, and (G) any shares of our common stock issuable upon conversion of the Company's 3.00% Convertible Senior Notes due 2022 provided that the aggregate number of shares of stock issued pursuant to clause (F) shall not exceed 10.0% of the total number of outstanding shares of our common stock immediately following the issuance and sale of shares of our common stock pursuant to the underwriting agreement; provided, further, the recipient of any such shares of our common stock and securities issued pursuant to clauses (C), (E) or (F) during the 60-day restricted period described above shall enter into an agreement substantially in the form described below.

Our directors and executive officers have entered into lock-up agreements with the underwriter prior to the commencement of this offering pursuant to which each of these persons or entities, for a period of 60 days after the date of this prospectus, may not, without the prior written consent of RBC Capital Markets, LLC, (1) offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, or otherwise transfer or dispose of, directly or indirectly, any shares of our common stock or any securities convertible into or exercisable or exchangeable for our common stock (including, without limitation, common stock or such other securities which may be deemed to be beneficially owned by such directors, executive officers, managers and members in accordance with the rules and regulations of the SEC and securities which may be issued upon exercise of a stock option or warrant) or publicly disclose the intention to make any offer, sale, pledge or disposition or (2) enter into any swap or other agreement that transfers, in whole or in

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part, any of the economic consequences of ownership of our common stock or such other securities, whether any such transaction described in clause (1) or (2) above is to be settled by delivery of common stock or such other securities, in cash or otherwise, or (3) make any demand for or exercise any right with respect to the registration of any shares of our common stock or any security convertible into or exercisable or exchangeable for our common stock, in each case subject to certain exceptions, including, among others, (A) shares of common stock to be sold pursuant to the underwriting agreement, (B) transfers of shares of common stock or other securities as bona fide gifts, (C) transfers or dispositions of shares of common stock or other securities to any trust for the direct or indirect benefit of the director, officer or stockholder or the immediate family of such person in a transaction not involving a disposition for value, (D) transfers or dispositions of shares of common stock or other securities to any affiliate of the director, officer or stockholder or to any investment fund or other entity controlled or managed by such director, officer or stockholder, (E) transfers or dispositions of shares of common stock or other securities by will, other testamentary document or intestate succession to the legal representative, heir, beneficiary or a member of the immediate family of the director, officer or stockholder, (F) distributions of shares of common stock or other securities to any of the stockholder's partners, members or stockholders, provided that certain limitations on filings under the Exchange Act or other public announcements reporting a reduction in the beneficial ownership of common stock held by the director, officer or stockholder apply in connection with such transfer or disposition. In the case of any transfer, disposition or distribution pursuant to clause (B), (C), (D), (E) or (F), each transferee, donee or distributee must execute and deliver to RBC Capital Markets, LLC a lock-up agreement. In addition, notwithstanding the foregoing restrictions, the director, officer or stockholder may (i) exercise an option to purchase shares of common stock granted under any stock incentive plan or stock purchase plan, provided that the underlying shares of common stock continue to be subject to the restrictions on transfer set forth in the lock-up agreement, (ii) transfer such stockholder's common stock or any security convertible into or exercisable or exchangeable for common stock to us pursuant to any contractual arrangement in effect on the date of the lock-up agreement that provides for the repurchase of such stockholder's common stock or such other securities by us or in connection with the termination of such stockholder's employment with us, (iii) establish a trading plan pursuant to Rule 10b5-1 under the Exchange Act for the transfer of common stock, provided that such plan does not provide for any transfers of common stock, and no filing with the SEC or other public announcement shall be required or voluntarily made by the director, officer or stockholder or any other person in connection therewith, in each case during the 60-day restricted period pursuant to the lock-up agreement, (iv) transfer or sell shares of such stockholder's common stock pursuant to a trading plan under Rule 10b5-1 under the Exchange Act that was established on or prior to the date of the lock-up agreement and exists as of the date of the lock-up agreement, and (v) transfer or dispose of shares of common stock acquired in this offering, subject to certain restrictions with respect to company directed shares, or on the open market following the offering, provided that certain limitations on filings under the Exchange Act or other public announcements reporting a reduction in the beneficial ownership of common stock held by the director, officer or stockholder apply in connection with such transfer or disposition.

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

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Our common stock is listed on The Nasdaq Global Select Market under the symbol "PTCT".

In connection with this offering, the underwriter may engage in stabilizing transactions, which involves making bids for, purchasing and selling shares of our 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 the common stock, which involves the sale by the underwriter of a greater number of shares of our common stock than they are required to purchase in this offering, and purchasing shares of our 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 underwriter's option referred to above, or may be "naked" shorts, which are short positions in excess of that amount. The underwriter may close out any covered short position either by exercising its option, in whole or in part, or by purchasing shares in the open market. In making this determination, the underwriter will consider, among other things, the price of shares available for purchase in the open market compared to the price at which the underwriter may purchase shares through the option. A naked short position is more likely to be created if the underwriter is 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 underwriter creates a naked short position, it will purchase shares in the open market to cover the position.

The underwriter has advised us that, pursuant to Regulation M of the Securities Act of 1933, it may also engage in other activities that stabilize, maintain or otherwise affect the price of the common stock.

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 underwriter commences these activities, it may discontinue them at any time. The underwriter may carry out these transactions on The Nasdaq Global Select Market, in the over the counter market or otherwise.

In addition, in connection with this offering, the underwriter may engage in passive market making transactions in our common stock on The Nasdaq Global Select Market prior to the pricing and completion of this offering. Passive market making consists of displaying bids on The Nasdaq Global Select Market no higher than the bid prices of independent market makers and making purchases at prices no higher than these independent bids and effected in response to order flow. Net purchases by a passive market maker on each day are generally limited to a specified percentage of the passive market maker's average daily trading volume in the common stock during a specified period and must be discontinued when such limit is reached. Passive market making may cause the price of our common stock to be higher than the price that otherwise would exist in the open market in the absence of these transactions. If passive market making is commenced, it may be discontinued at any time.

Other than in the United States, no action has been taken by us or the underwriter 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

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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.

The underwriter and its affiliates are full service financial institutions engaged in various activities, which may include sales and trading, commercial and investment banking, advisory, investment management, investment research, principal investment, hedging, market making, brokerage and other financial and non-financial activities and services. The underwriter and its 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, the underwriter and its 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.

Selling restrictions

Canada

Our common 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 our common 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 underwriter is not required to comply with the disclosure requirements of NI 33-105 regarding underwriter conflicts of interest in connection with this offering.

European Economic Area

In relation to each Member State of the European Economic Area that has implemented the Prospectus Directive (each, a "Relevant Member State"), an offer to the public of our common shares may not be made in that Relevant Member State, except that an offer to the public in that

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Relevant Member State of our common shares may be made at any time under the following exemptions under the Prospectus Directive:

(a) to any legal entity that is a qualified investor as defined in the Prospectus Directive;

(b) to fewer than 150 natural or legal persons (other than qualified investors as defined in the Prospectus Directive), subject to obtaining the prior consent of the Representatives for any such offer; or

(c) in any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer of shares of our common stock shall result in a requirement for the publication by us or any underwriter of a prospectus pursuant to Article 3 of the Prospectus Directive.

For the purposes of this provision, the expression an "offer to the public" in relation to our common shares in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and our common shares to be offered so as to enable an investor to decide to purchase our common shares, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State; and the expression "Prospectus Directive" means Directive 2003/71/EC (as amended), including by Directive 2010/73/EU, and includes any relevant implementing measure in the Relevant Member State.

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 Directive) (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 our common 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.

Australia

No placement document, prospectus, product disclosure statement or other disclosure document has been lodged with the Australian Securities and Investments Commission ("ASIC"), in relation to this offering. This prospectus supplement and accompanying prospectus does not constitute a prospectus, product disclosure statement or other disclosure document under the Corporations Act 2001 (the "Corporations Act"), and does not purport to include the information

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required for a prospectus, product disclosure statement or other disclosure document under the Corporations Act.

Any offer in Australia of our common shares may only be made to persons (the "Exempt Investors") who are "sophisticated investors" (within the meaning of section 708(8) of the Corporations Act), "professional investors" (within the meaning of section 708(11) of the Corporations Act) or otherwise pursuant to one or more exemptions contained in section 708 of the Corporations Act so that it is lawful to offer our common shares without disclosure to investors under Chapter 6D of the Corporations Act.

The common shares applied for by Exempt Investors in Australia must not be offered for sale in Australia in the period of 12 months after the date of allotment under this offering, except in circumstances where disclosure to investors under Chapter 6D of the Corporations Act would not be required pursuant to an exemption under section 708 of the Corporations Act or otherwise or where the offer is pursuant to a disclosure document which complies with Chapter 6D of the Corporations Act. Any person acquiring our common shares must observe such Australian on-sale restrictions.

This prospectus supplement and accompanying prospectus contain general information only and does not take account of the investment objectives, financial situation or particular needs of any particular person. It does not contain any securities recommendations or financial product advice. Before making an investment decision, investors need to consider whether the information in this prospectus supplement and accompanying prospectus is appropriate to their needs, objectives and circumstances, and, if necessary, seek expert advice on those matters.

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MATERIAL FEDERAL U.S. TAX CONSIDERATIONS FOR NON-U.S. HOLDERS OF COMMON STOCK

The following is a general discussion of material U.S. federal income and estate tax considerations relating to ownership and disposition of our common stock by a non-U.S. holder. For purposes of this discussion, the term "non-U.S. holder" means a beneficial owner of our common stock 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 other entity treated as a corporation for U.S. federal income tax purposes, created or organized in or under the laws of the United States or of any political subdivision of the United States;
- an estate the income of which is subject to U.S. federal income taxation regardless of its source; or
- a trust, if a U.S. court is able to exercise primary supervision over the administration of the trust and one or more U.S. persons have authority to control all substantial decisions of the trust or if the trust has a valid election in effect under applicable U.S. Treasury Regulations to be treated as a U.S. person.

This discussion does not address the tax treatment of partnerships or persons who hold their common stock through partnerships or other entities that are pass-through entities for U.S. federal income tax purposes. A partner in a partnership or other pass-through entity that will hold our common stock should consult his, her or its own tax advisor regarding the tax consequences of the ownership and disposition of our common stock through a partnership or other pass-through entity, as applicable.

This discussion is based on current provisions of the U.S. Internal Revenue Code of 1986, as amended, or the Code, existing and proposed U.S. Treasury Regulations promulgated thereunder, current administrative rulings and judicial decisions, all as in effect as of the date of this prospectus and all of which are subject to change or to differing interpretation, possibly with retroactive effect. Any change could alter the tax consequences to non-U.S. holders described in this prospectus. In addition, the Internal Revenue Service, or the IRS, could challenge one or more of the tax consequences described in this prospectus.

We assume in this discussion that each non-U.S. holder holds shares of our common stock as a capital asset (generally, property held for investment) for U.S. federal income tax purposes. This discussion does not address all aspects of U.S. federal income and estate 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. state, local or non-U.S. taxes, the alternative minimum tax, or the Medicare tax on net investment income. 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:

- insurance companies;
- tax-exempt organizations;
- financial institutions;

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brokers or dealers in securities;

pension plans;

controlled foreign corporations;

passive foreign investment companies;

non-U.S. governments;

owners that hold our common stock as part of a straddle, hedge, conversion transaction, synthetic security or other integrated investment or who have elected to mark securities to market for U.S. federal income tax purposes; and

certain U.S. expatriates.

THIS SUMMARY IS FOR GENERAL INFORMATION ONLY AND IS NOT, AND IS NOT INTENDED TO BE, LEGAL OR TAX ADVICE. PROSPECTIVE INVESTORS SHOULD CONSULT THEIR OWN TAX ADVISORS REGARDING THE U.S. FEDERAL, STATE, LOCAL AND NON-U.S. TAX CONSIDERATIONS OF ACQUIRING, HOLDING AND DISPOSING OF OUR COMMON STOCK.

Distributions

As discussed under "Dividend Policy" above, we do not currently expect to make distributions in respect of our common stock. If we make distributions in respect of our common stock, those distributions 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, subject to the tax treatment described in this section. If a distribution exceeds our current and accumulated earnings and profits, the excess will be treated as a tax-free return of capital, up to the holder's tax basis in the common stock. Any remaining excess will be treated as capital gain, subject to the tax treatment described below under the heading "Gain on Sale, Exchange or Other Taxable Disposition of Our Common Stock." Distributions will also be subject to the discussion below under the heading "FATCA."

Dividends paid to a non-U.S. holder generally will 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 between the United States and such holder's country of residence.

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 (generally including provision of 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, dividends that are treated as U.S. effectively connected income, net of specified deductions and credits, are taxed in the hands of the non-U.S. holder at the same U.S. federal income tax rates as would apply if such holder were a U.S. person (as defined in the Code). Any U.S. effectively connected income received by a non-U.S. holder that is classified as a corporation for U.S. federal income tax purposes may also, under certain circumstances, be subject to an

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additional "branch profits tax" at a 30% rate or such lower rate as may be specified by an applicable income tax treaty between the United States and such holder's country of residence.

A non-U.S. holder of our common stock who claims the benefit of an applicable income tax treaty between the United States and such holder's country of residence generally will be required to provide a properly executed IRS Form W-8BEN or W-8BEN-E (or successor form) and satisfy applicable certification and other requirements.

Each non-U.S. holder is urged to consult its own tax advisor about the specific methods for satisfying these requirements and regarding its entitlement to benefits under a relevant 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 a refund or credit with the IRS.

Gain on Sale, Exchange or Other Taxable Disposition of Our Common Stock

Subject to the discussion below under the heading "FATCA," a non-U.S. holder generally will not be subject to U.S. federal income tax or withholding tax on gain recognized on a disposition of our common stock unless:

- the gain is effectively connected with the non-U.S. holder's conduct of a trade or business in the United States, and, if an applicable income tax treaty so provides, the gain is attributable to a permanent establishment or fixed base maintained by the non-U.S. holder in the United States; in this case, the non-U.S. holder will be taxed on a net income basis at the same rates as would apply if it were a U.S. person, and, if the non-U.S. holder is a foreign corporation, an additional branch profits tax at a rate of 30%, or a lower rate as may be specified by an applicable income tax treaty, may also apply;

- the non-U.S. holder is a nonresident alien present in the United States for 183 days or more in the taxable year of the disposition and certain other requirements 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 certain U.S.-source capital losses of the non-U.S. holder recognized in the taxable year of the disposition, if any; or

- 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" unless our common stock is regularly traded on an established securities market and the non-U.S. holder held no more than 5% of our outstanding common stock, directly or indirectly, 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. We believe that we are not currently, and we do not anticipate becoming, a "U.S. real property holding corporation" for U.S. federal income tax purposes.

Information Reporting and Backup Withholding

We or a financial intermediary must report annually to the IRS and to each non-U.S. holder the gross amount of the distributions on our common stock paid to such holder and the tax withheld, if any, with respect to such distributions. A non-U.S. holder generally will have to

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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. Generally, a holder will comply with such procedures if it provides a properly executed IRS Form W-8BEN or W-BEN-E (or other applicable Form W-8), and the payor does not have actual knowledge or reason to know that such holder is a U.S. person as defined under the Code, or otherwise meets documentary evidence requirements for establishing that it is a non-U.S. holder, or otherwise establishes an exemption. Dividends paid to non-U.S. holders subject to withholding of U.S. federal income tax, as described above under "Distributions," will generally be exempt from U.S. backup withholding.

Information reporting and backup withholding generally will 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 non-U.S., unless the holder certifies that it is not a "United States person" (as defined in the Code) 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-United States person 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 can be refunded or credited against the non-U.S. holder's U.S. federal income tax liability, if any, provided that an appropriate claim is timely filed with the IRS.

FATCA

Provisions of the Code commonly referred to as the Foreign Account Tax Compliance Act, or FATCA, generally impose a 30% withholding tax on dividends on, and gross proceeds from the sale or disposition of, our common stock if paid to a foreign entity unless (i) if the foreign entity is a "foreign financial institution," the foreign entity undertakes certain due diligence, reporting, withholding, and certification obligations, (ii) if the foreign entity is not a "foreign financial institution," the foreign entity identifies certain of its U.S. investors, or (iii) the foreign entity is otherwise exempt under FATCA.

Withholding under FATCA generally applies to payments of dividends on our common stock. While withholding under FATCA may apply to payments of gross proceeds from a sale or other disposition of our common stock, under recently proposed U.S. Treasury Regulations withholding on payments of gross proceeds is not required. Although these regulations are not final, applicable withholding agents may rely on the proposed regulations until final regulations are issued.

An intergovernmental agreement between the United States and an applicable foreign country may modify the requirements described in this section. Under certain circumstances, a non-U.S.

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holder may be eligible for refunds or credits of the tax. Non-U.S. holders should consult their own tax advisors regarding the possible implications of FATCA on their investment in our common stock.

Federal Estate Tax

Common stock owned or treated as owned by an individual who is not a citizen or resident of the United States (as specially defined for U.S. federal estate tax purposes) at the time of death will be included in the individual's gross estate for U.S. federal estate tax purposes and, therefore, may be subject to U.S. federal estate tax, unless an applicable estate tax or other treaty provides otherwise.

The preceding discussion of material U.S. federal income and estate tax considerations is for general information only. It is not legal or tax advice. Prospective investors should consult their own tax advisors regarding the particular U.S. federal, state, local and non-U.S. tax consequences of purchasing, holding and disposing of our common stock, including the consequences of any proposed changes in applicable laws.

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LEGAL MATTERS

The validity of the shares of common stock offered hereby will be passed upon for us by Wilmer Cutler Pickering Hale and Dorr LLP. The underwriter is being represented in connection with this offering by Davis Polk & Wardwell LLP, New York, New York.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2017, and the effectiveness of our internal control over financial reporting as of December 31, 2017, as set forth in their reports, which are incorporated by reference in this prospectus supplement and elsewhere in the registration statement. Our financial statements are incorporated by reference in reliance on Ernst & Young LLP's reports, given on their authority as experts in accounting and auditing.

The financial statements of Agilis Biotherapeutics, Inc. as of and for the years ended December 31, 2017 and 2016, incorporated in this prospectus by reference from our Current Report on Form 8-K filed August 24, 2018 have been audited by BDO USA, LLP, independent auditors, as stated in their report, which is incorporated herein by reference. Such financial statements have been so incorporated in reliance upon the report of such firm given upon their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

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. Copies of certain information filed by us with the SEC are also available on our website at http://www.ptcbio.com. Our website is not a part of this prospectus and is not incorporated by reference in this prospectus.

This prospectus supplement is part of a registration statement we filed with the SEC. This prospectus supplement and the accompanying prospectus omit some information contained in the registration statement in accordance with SEC rules and regulations. You should review the information and exhibits in the registration statement for further information on us and our consolidated subsidiaries and the securities we are offering. Statements in this prospectus supplement and the accompanying prospectus concerning any document we filed as an exhibit to the registration statement or that we otherwise filed with the SEC are not intended to be comprehensive and are qualified by reference to these filings. You should review the complete document to evaluate these statements. You can obtain a copy of the registration statement from the SEC at the address listed above or from the SEC's Internet site.

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INCORPORATION BY REFERENCE

The SEC allows us to incorporate by reference much of the information we file with the SEC, which means that we can disclose important information to you by referring you to those publicly available documents. The information that we incorporate by reference in this prospectus supplement and the accompanying prospectus is considered to be part of this prospectus supplement and the accompanying prospectus. Because we are incorporating by reference future filings with the SEC, this prospectus supplement and the accompanying prospectus are continually updated and those future filings may modify or supersede some of the information included or incorporated in this prospectus supplement and the accompanying prospectus. This means that you must look at all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus supplement, the accompanying prospectus or in any document previously incorporated by reference have been modified or superseded. This prospectus supplement and the accompanying prospectus incorporate by reference the documents listed below (File No. 001-35969) and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended (in each case, other than those documents or the portions of those documents not deemed to be filed), until the offering of the securities under the registration statement is terminated or completed:

- Annual Report on Form 10-K for the fiscal year ended December 31, 2017;
- the information specifically incorporated by reference into our Annual Report on Form 10-K for the fiscal year ended December 31, 2017 from our definitive proxy statement for the 2018 Annual Meeting of Shareholders, filed on April 30, 2018;
- Quarterly Reports on Form 10-Q for the fiscal quarters ended March 31, 2018, June 30, 2018 and September 30, 2018;
- Current Reports on Form 8-K filed on February 20, 2018, April 3, 2018, June 14, 2018, July 19, 2018 (excluding Item 7.01 and Exhibit 99.1), August 2, 2018 (excluding Item 7.01 and Exhibit 99.1), August 24, 2018 (excluding Item 7.01 and Exhibit 99.1), August 28, 2018, October 5, 2018 and December 18, 2018 (excluding Item 7.01 and Exhibit 99.1); and
- the description of the securities contained in our registration statement on Form 8-A filed on June 14, 2013, including any amendment or report filed for the purpose of updating such description.

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

PTC Therapeutics, Inc.
100 Corporate Court
South Plainfield, New Jersey 07080
(908) 222-7000

PROSPECTUS

PTC Therapeutics, Inc.

Debt Securities
Common Stock
Preferred Stock
Depositary Shares
Purchase Contracts
Purchase Units
Warrants

We may issue securities from time to time in one or more offerings. This prospectus describes the general terms of these securities and the general manner in which these securities will be offered. We will provide the specific terms of these securities in supplements to this prospectus. The prospectus supplements will also describe the specific manner in which these securities will be offered and may also supplement, update or amend information contained in this document. This prospectus may be used to offer shares of our common stock for the account of persons other than us, whom we refer to in this prospectus as "selling stockholders." You should read this prospectus and any applicable prospectus supplement carefully before you invest.

We or any selling stockholders may offer these securities in amounts, at prices and on terms determined at the time of offering. The securities may be sold directly to you, through agents, or through underwriters and dealers. If agents, underwriters or dealers are used to sell the securities, we will name them and describe their compensation in a prospectus supplement. Unless otherwise set forth in a prospectus supplement, we will not receive any proceeds from the sale of common stock by any selling stockholders.

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

Investing in these securities involves significant risks. See the information contained in this prospectus under the heading "Risk Factors" beginning on page 2, in any accompanying prospectus supplement and in the documents incorporated by reference in this prospectus for a discussion of the factors you should carefully consider before deciding to purchase these securities.

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

The date of this prospectus is August 24, 2017.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, which we refer to as the SEC, utilizing a "shelf" registration process. Under this shelf registration process, we may from time to time sell any combination of the securities described in this prospectus in one or more offerings, and selling stockholders may from time to time sell shares of common stock described in this prospectus in one or more offering.

This prospectus provides you with a general description of the securities we or selling stockholders may offer. Each time we or selling stockholders sell securities, we will provide one or more prospectus supplements that will contain specific information about the terms of the offering. The prospectus supplement may also add, update or change information contained in this prospectus. You should read both this prospectus and the accompanying prospectus supplement together with the additional information described under the heading "Where You Can Find More Information" beginning on page 2 of this prospectus.

We have not authorized anyone to provide you with information different from that contained in this prospectus, any accompanying prospectus supplement or in any related free writing prospectus filed by us with the SEC. We do not take any responsibility for, and cannot provide any assurance as to the reliability of, any information other than the information in this prospectus, any accompanying prospectus supplement or in any related free writing prospectus filed by us with the SEC. This prospectus and the accompanying prospectus supplement do not constitute an offer to sell or the solicitation of an offer to buy any securities other than the securities described in the accompanying prospectus supplement or an offer to sell or the solicitation of an offer to buy such securities in any circumstances in which such offer or solicitation is unlawful. You should assume that the information appearing in this prospectus, any prospectus supplement, the documents incorporated by reference and any related free writing prospectus is accurate only as of their respective dates. Our business, financial condition, results of operations and prospects may have changed materially since those dates.

Unless the context otherwise indicates, references in this prospectus to "PTC," "we," "our," "us" and "the Company" refer, collectively, to PTC Therapeutics, Inc., a Delaware corporation, and its consolidated subsidiaries.

RISK FACTORS

Investing in our securities involves significant risks. You should carefully consider the risks and uncertainties described in this prospectus and any accompanying prospectus supplement, including the risk factors set forth in our filings with the SEC that are incorporated by reference herein, before making an investment decision pursuant to this prospectus and any accompanying prospectus supplement relating to a specific offering.

Our business, financial condition and results of operations could be materially and adversely affected by any or all of these risks or by additional risks and uncertainties not presently known to us or that we currently deem immaterial that may adversely affect us in the future.

WHERE YOU CAN FIND MORE INFORMATION

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. Copies of certain information filed by us with the SEC are also available on our website at http://www.ptcbio.com. Our website is not a part of this prospectus and is not incorporated by reference in this prospectus. You may also read and copy any document we file at the SEC's Public Reference Room, 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the Public Reference Room.

This prospectus is part of a registration statement we filed with the SEC. This prospectus omits some information contained in the registration statement in accordance with SEC rules and regulations. You should review the information and exhibits in the registration statement for further information on us and our consolidated subsidiaries and the securities we are offering. Statements in this prospectus concerning any document we filed as an exhibit to the registration statement or that we otherwise filed with the SEC are not intended to be comprehensive and are qualified by reference to these filings. You should review the complete document to evaluate these statements. You can obtain a copy of the registration statement from the SEC at the address listed above or from the SEC's website.

INCORPORATION BY REFERENCE

The SEC allows us to incorporate by reference in this prospectus much of the information we file with the SEC, which means that we can disclose important information to you by referring you to those publicly available documents. The information that we incorporate by reference in this prospectus is considered to be part of this prospectus. Because we are incorporating by reference future filings with the SEC, this prospectus is continually updated and those future filings may modify or supersede some of the information included or incorporated in this prospectus. This means that you must look at all of the SEC filings that we incorporate by reference to determine if any of the statements in this prospectus or in any document previously incorporated by reference have been modified or superseded. This prospectus incorporates by reference the documents listed below (File No. 001-35969) and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934, as amended, or the Exchange Act (in each case, other than those documents or the portions of those documents not deemed to be filed) until the offering of the securities under the registration statement is terminated or completed:

Annual Report on Form 10-K for the fiscal year ended December 31, 2016, including the information specifically incorporated by reference into the Annual Report on Form 10-K from our definitive proxy statement for the 2017 Annual Meeting of Stockholders;

Quarterly Reports on Form 10-Q for the fiscal quarters ended March 31, 2017 and June 30, 2017;

Current Reports on Form 8-K filed on March 2, 2017 (solely with respect to Item 8.01), March 16, 2017 (solely with respect to Items 1.01 and 3.02), April 10, 2017, April 17, 2017, April 20, 2017 (solely with respect to Items 2.01, 3.02 and 9.01, as amended on July 3, 2017), April 21, 2017, May 8, 2017 (solely with respect to Items 1.01, 2.03 and 9.01), June 5, 2017 (solely with respect to Item 5.02), June 12, 2017 and August 8, 2017 (solely with respect to Item 5.02); and

The description of the securities contained in our registration statement on Form 8-A filed under the Exchange Act on June 14, 2013, including any amendment or report filed for the purpose of updating such description.

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

PTC Therapeutics, Inc.
100 Corporate Court
South Plainfield, New Jersey 07080
(908) 222-7000

FORWARD-LOOKING STATEMENTS

This prospectus and the information incorporated by reference in this prospectus include "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933, as amended, or the Securities Act, and Section 21E of the Exchange Act. All statements contained or incorporated by reference herein, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans, objectives of management and expected market growth, other than statements of historical facts, are forward-looking statements. The words "anticipate," "believe," "estimate," "expect," "intend," "may," "might," "plan," "predict," "project," "potential," "will," "would," "could," "should," "continue," and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. We cannot guarantee that we actually will achieve the plans, intentions or expectations expressed or implied in our forward-looking statements. There are a number of important factors that could cause actual results, levels of activity, performance or events to differ materially from those expressed or implied in the forward-looking statements we make. These important factors include our "critical accounting estimates" described in Part II, Item 7 "Management's Discussion and Analysis of Financial Condition and Results of Operations Critical Accounting Policies and Significant Judgments and Estimates" of our Annual Report on Form 10-K for the fiscal year ended December 31, 2016 and the factors set forth under the caption "Risk Factors" in Part I, Item 1A of our Annual Report on Form 10-K for the fiscal year ended December 31, 2016 and under the caption "Risk Factors" in Part II, Item 1A of our Quarterly Reports on Form 10-Q for the fiscal quarters ended March 31, 2017 and June 30, 2017. Although we may elect to update forward-looking statements in the future, we specifically disclaim any obligation to do so, even if our estimates change, and readers should not rely on those forward-looking statements as representing our views as of any date subsequent to the date of this prospectus

THE COMPANY

We are a global biopharmaceutical company focused on the discovery, development, and commercialization of novel medicines using our expertise in RNA biology. Our internally discovered pipeline addresses multiple therapeutic areas, including rare disorders and oncology. We have discovered all of our compounds currently under development using our proprietary technologies. We plan to continue to develop these compounds both on our own and through selective collaboration arrangements with leading pharmaceutical and biotechnology companies. We have two products, Translarna (ataluren) and EMFLAZA (deflazacort). Translarna received marketing authorization from the European Commission in August 2014 for the treatment of nonsense mutation Duchenne muscular dystrophy in ambulatory patients age five years and older in the 31 member states of the European Economic Area. EMFLAZA is approved in the United States for the treatment of Duchenne muscular dystrophy in patients five years and older.

Our principal executive offices are located at 100 Corporate Court, South Plainfield, New Jersey 07080, and our telephone number is (908) 222-7000.

CONSOLIDATED RATIOS OF EARNINGS TO FIXED CHARGES

The following table sets forth our consolidated ratio of earnings to fixed charges for each of the periods indicated. For purposes of calculating the ratios in the table below, earnings consist of net loss plus fixed charges. Fixed charges include interest expensed and capitalized, amortized premiums, discounts and capitalized expenses related to indebtedness, an estimate of the interest within rental expense, and preference security dividend requirements of consolidated subsidiaries.

You should read this table in conjunction with the consolidated financial statements and notes incorporated by reference in this prospectus.

	Six Months Ended June 30,	Fiscal Year Ended December 31,				
	2017	2016	2015	2014	2013	2012
Consolidated ratios of earnings to fixed charges(1)(2)(3)	N/A	N/A	N/A	N/A	N/A	N/A

(1) Due to our losses for the six months ended June 30, 2017 and the years ended December 31, 2016, 2015, 2014, 2013 and 2012, the ratio coverage was less than 1:1.

(2) We would have needed to generate additional earnings of $46.2 million for the six months ended June 30, 2017 and $141.5 million, $170.0 million, $98.4 million, $51.6 million and $26.2 million for the years ended December 31, 2016, 2015, 2014, 2013 and 2012, respectively, to cover our fixed charges in those periods.

(3) Our consolidated ratios of earnings to combined fixed charges and preferred stock dividends for the periods indicated above are the same as our consolidated ratios of earnings to fixed charges set forth above.

USE OF PROCEEDS

We intend to use the net proceeds from the sale of any securities offered under this prospectus for general corporate purposes unless otherwise indicated in the applicable prospectus supplement. General corporate purposes may include research and development costs, the acquisition or licensing of other products, businesses or technologies, repayment and refinancing of debt, working capital and capital expenditures. We may temporarily invest the net proceeds in a variety of capital preservation instruments, including short-term, investment grade, interest bearing instruments and U.S. government securities, until they are used for their stated purpose. We have not determined the amount of net proceeds to be used specifically for such purposes. As a result, management will retain broad discretion over the allocation of net proceeds.

Unless otherwise set forth in a prospectus supplement, we will not receive any proceeds from the sale of common stock by any selling stockholders.

SELLING STOCKHOLDERS

In addition to covering the offering of the securities by us, this prospectus covers the offering for resale of common stock by selling stockholders. Information about selling stockholders, if any, will be set forth in a prospectus supplement, in an amendment to the registration statement of which this prospectus is a part or in other filings we make with the SEC under the Exchange Act, which are incorporated by reference.

DESCRIPTION OF DEBT SECURITIES

We may offer debt securities, which may be senior or subordinated. We refer to the senior debt securities and the subordinated debt securities collectively as debt securities. The following description summarizes the general terms and provisions of the debt securities. We will describe the specific terms of the debt securities and the extent, if any, to which the general provisions summarized below apply to any series of debt securities in the prospectus supplement relating to the series and any applicable free writing prospectus that we authorize to be delivered. When we refer to "PTC," "the Company," "we," "our," and "us" in this section, we mean PTC Therapeutics, Inc. excluding, unless the context otherwise requires or as otherwise expressly stated, our subsidiaries.

We may issue senior debt securities from time to time, in one or more series under a senior indenture to be entered into between us and a senior trustee to be named in a prospectus supplement, which we refer to as the senior trustee. We may issue subordinated debt securities from time to time, in one or more series under a subordinated indenture to be entered into between us and a subordinated trustee to be named in a prospectus supplement, which we refer to as the subordinated trustee. The forms of senior indenture and subordinated indenture are filed as exhibits to the registration statement of which this prospectus forms a part. Together, the senior indenture and the subordinated indenture are referred to as the indentures and, together, the senior trustee and the subordinated trustee are referred to as the trustees. This prospectus briefly outlines some of the provisions of the indentures. The following summary of the material provisions of the indentures is qualified in its entirety by the provisions of the indentures, including definitions of certain terms used in the indentures. Wherever we refer to particular sections or defined terms of the indentures, those sections or defined terms are incorporated by reference in this prospectus or the applicable prospectus supplement. You should review the indentures that are filed as exhibits to the registration statement of which this prospectus forms a part for additional information.

None of the indentures will limit the amount of debt securities that we may issue. The applicable indenture will provide that debt securities may be issued up to an aggregate principal amount authorized from time to time by us and may be payable in any currency or currency unit designated by us or in amounts determined by reference to an index.

General

The senior debt securities will constitute our unsubordinated general obligations and will rank pari passu with our other unsubordinated obligations. The subordinated debt securities will constitute our subordinated general obligations and will be junior in right of payment to our senior indebtedness (including senior debt securities), as described under the heading " Certain Terms of the Subordinated Debt Securities Subordination."

The debt securities will be our unsecured obligations unless otherwise specified in the applicable prospectus supplement. Any secured debt or other secured obligations will be effectively senior to the debt securities to the extent of the value of the assets securing such debt or other obligations.

The applicable prospectus supplement and any free writing prospectus will include any additional or different terms of the debt securities or any series being offered, including the following terms:

- the title and type of the debt securities;
- whether the debt securities will be senior or subordinated debt securities, and, with respect to debt securities issued under the subordinated indenture, the terms on which they are subordinated;
- the aggregate principal amount of the debt securities;
- the price or prices at which we will sell the debt securities;

the maturity date or dates of the debt securities and the right, if any, to extend such date or dates;

the rate or rates, if any, per year, at which the debt securities will bear interest, or the method of determining such rate or rates;

the date or dates from which such interest will accrue, the interest payment dates on which such interest will be payable or the manner of determination of such interest payment dates and the related record dates;

the right, if any, to extend the interest payment periods and the duration of that extension;

the manner of paying principal and interest and the place or places where principal and interest will be payable;

provisions for a sinking fund, purchase fund or other analogous fund, if any;

any redemption dates, prices, obligations and restrictions on the debt securities;

the currency, currencies or currency units in which the debt securities will be denominated and the currency, currencies or currency units in which principal and interest, if any, on the debt securities may be payable;

any conversion or exchange features of the debt securities;

whether and upon what terms the debt securities may be defeased;

any events of default or covenants in addition to or in lieu of those set forth in the indenture;

whether the debt securities will be issued in definitive or global form or in definitive form only upon satisfaction of certain conditions;

whether debt securities will be guaranteed as to payment or performance;

if the debt securities of the series or, if applicable, any guarantees will be secured by any collateral and, if so, a general description of the collateral and the terms and provisions of such collateral security, pledge or other agreements; and

any other material terms of the debt securities.

The applicable prospectus supplement will also describe any applicable material U.S. federal income tax consequences.

When we refer to "principal" in this section with reference to the debt securities, we are also referring to "premium", if any.

We may from time to time, without notice to or the consent of the holders of any series of debt securities, create and issue further debt securities of any such series ranking equally with the debt securities of such series in all respects (or in all respects other than (1) the payment of interest accruing prior to the issue date of such further debt securities or (2) the first payment of interest following the issue date of such further debt securities). Such further debt securities may be consolidated and form a single series with the debt securities of such series and have the

same terms as to status, redemption or otherwise as the debt securities of such series.

You may present debt securities for exchange and you may present debt securities for transfer in the manner, at the places and subject to the restrictions set forth in the debt securities and the applicable prospectus supplement. We will provide you those services without charge, although you may have to pay any tax or other governmental charge payable in connection with any exchange or transfer, as set forth in the indenture.

Debt securities may bear interest at a fixed rate or a floating rate. Debt securities bearing no interest or interest at a rate that at the time of issuance is below the prevailing market rate (original issue discount securities) may be sold at a discount below their stated principal amount.

We may issue debt securities with the principal amount payable on any principal payment date, or the amount of interest payable on any interest payment date, to be determined by reference to one or more currency exchange rates, securities or baskets of securities, commodity prices or indices. You may receive a payment of principal on any principal payment date, or a payment of interest on any interest payment date, that is greater than or less than the amount of principal or interest otherwise payable on such dates, depending on the value on such dates of the applicable currency, security or basket of securities, commodity or index. Information as to the methods for determining the amount of principal or interest payable on any date, the currencies, securities or baskets of securities, commodities or indices to which the amount payable on such date is linked.

Certain Terms of the Senior Debt Securities

Covenants. Unless we indicate otherwise in a prospectus supplement, the senior debt securities will not contain any financial or restrictive covenants, including covenants restricting either us or any of our subsidiaries from incurring, issuing, assuming or guaranteeing any indebtedness secured by a lien on any of our or our subsidiaries' property or capital stock, or restricting either us or any of our subsidiaries from entering into sale and leaseback transactions.

Consolidation, Merger and Sale of Assets. Unless we indicate otherwise in a prospectus supplement, we may not consolidate with or merge into any other person, in a transaction in which we are not the surviving corporation, or convey, transfer or lease our properties and assets substantially as an entirety to any person, in either case, unless:

- the successor entity, if any, is a U.S. corporation, limited liability company, partnership or trust (subject to certain exceptions provided for in the senior indenture);
- the successor entity assumes our obligations on the senior debt securities and under the senior indenture;
- immediately after giving effect to the transaction, no default or event of default shall have occurred and be continuing; and
- certain other conditions are met.

No Protection in the Event of a Change in Control. Unless we indicate otherwise in a prospectus supplement with respect to a particular series of senior debt securities, the senior debt securities will not contain any provisions that may afford holders of the senior debt securities protection in the event we have a change in control or in the event of a highly leveraged transaction (whether or not such transaction results in a change in control).

Events of Default. Unless we indicate otherwise in a prospectus supplement with respect to a particular series of senior debt securities, the following are events of default under the senior indenture for any series of senior debt securities:

- failure to pay interest on any senior debt securities of such series when due and payable, if that default continues for a period of 90 days (or such other period as may be specified for such series);
- failure to pay principal on the senior debt securities of such series when due and payable whether at maturity, upon redemption, by declaration or otherwise (and, if specified for such series, the continuance of such failure for a specified period);

default in the performance of or breach of any of our covenants or agreements in the senior indenture applicable to senior debt securities of such series, other than a covenant breach which is specifically dealt with elsewhere in the senior indenture, and that default or breach continues for a period of 90 days after we receive written notice from the trustee or from the holders of 25% or more in aggregate principal amount of the senior debt securities of such series;

certain events of bankruptcy or insolvency, whether or not voluntary; and

any other event of default provided for in such series of senior debt securities as may be specified in the applicable prospectus supplement.

Unless we indicate otherwise in a prospectus supplement, the default by us under any other debt, including any other series of debt securities, is not a default under the senior indenture.

If an event of default other than an event of default specified in the fourth bullet point above occurs with respect to a series of senior debt securities and is continuing under the senior indenture, then, and in each such case, either the trustee or the holders of not less than 25% in aggregate principal amount of such series then outstanding under the senior indenture (each such series voting as a separate class) by written notice to us and to the trustee, if such notice is given by the holders, may, and the trustee at the request of such holders shall, declare the principal amount of and accrued interest on such series of senior debt securities to be immediately due and payable, and upon this declaration, the same shall become immediately due and payable.

If an event of default specified in the fourth bullet point above occurs with respect to us and is continuing, the entire principal amount of and accrued interest, if any, on each series of senior debt securities then outstanding shall become immediately due and payable.

Unless otherwise specified in the prospectus supplement relating to a series of senior debt securities originally issued at a discount, the amount due upon acceleration shall include only the original issue price of the senior debt securities, the amount of original issue discount accrued to the date of acceleration and accrued interest, if any.

Upon certain conditions, declarations of acceleration may be rescinded and annulled and past defaults may be waived by the holders of a majority in aggregate principal amount of all the senior debt securities of such series affected by the default, each series voting as a separate class. Furthermore, subject to various provisions in the senior indenture, the holders of a majority in aggregate principal amount of a series of senior debt securities, by notice to the trustee, may waive an existing default or event of default with respect to such senior debt securities and its consequences, except an uncured default in the payment of principal of or interest on such senior debt securities or in respect of a covenant or provision of the senior indenture which cannot be modified or amended without the consent of the holders of each such senior debt security. Upon any such waiver, such default shall cease to exist, and any event of default with respect to such senior debt securities shall be deemed to have been cured, for every purpose of the senior indenture; but no such waiver shall extend to any subsequent or other default or event of default or impair any right consequent thereto. For information as to the waiver of defaults, see " Modification and Waiver."

The holders of a majority in aggregate principal amount of a series of senior debt securities may 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 such senior debt securities. However, the trustee may refuse to follow any direction that conflicts with law or the senior indenture, that may involve the trustee in personal liability or that the trustee determines in good faith may be unduly prejudicial to the rights of holders of such series of senior debt securities not joining in the giving of such direction and may take any other action it deems proper that is not inconsistent with any

such direction received from holders of such series of senior debt securities. A holder may not pursue any remedy with respect to the senior indenture or any series of senior debt securities unless:

- the holder gives the trustee written notice of a continuing event of default;
- the holders of at least 25% in aggregate principal amount of such series of senior debt securities make a written request to the trustee to pursue the remedy in respect of such event of default;
- the requesting holder or holders offer the trustee indemnity satisfactory to the trustee against any costs, liability or expense;
- the trustee does not comply with the request within 60 days after receipt of the request and the offer of indemnity; and
- during such 60-day period, the holders of a majority in aggregate principal amount of such series of senior debt securities do not give the trustee a direction that is inconsistent with the request.

These limitations, however, do not apply to the right of any holder of a senior debt security to receive payment of the principal of and interest, if any, on such senior debt security in accordance with the terms of such debt security, or to bring suit for the enforcement of any such payment in accordance with the terms of such debt security, on or after the due date for the senior debt securities, which right shall not be impaired or affected without the consent of the holder.

The senior indenture requires certain of our officers to certify, on or before a fixed date in each year in which any senior debt security is outstanding, as to their knowledge of our compliance with all covenants, agreements and conditions under the senior indenture.

Satisfaction and Discharge. We can satisfy and discharge our obligations to holders of any series of senior debt securities if:

- we pay or cause to be paid, as and when due and payable, the principal of and any interest on all senior debt securities of such series outstanding under the senior indenture; or
- all senior debt securities of such series have become due and payable or will become due and payable within one year (or are to be called for redemption within one year) and we deposit in trust a combination of cash and U.S. government or U.S. government agency obligations that will generate enough cash to make interest, principal and any other payments on the debt securities of that series on their various due dates.

Under current U.S. federal income tax law, the deposit and our legal release from the senior debt securities would be treated as a taxable event, and beneficial owners of such debt securities would generally recognize any gain or loss on such senior debt securities. Purchasers of the senior debt securities should consult their own advisers with respect to the tax consequences to them of such deposit and discharge, including the applicability and effect of tax laws other than the U.S. federal income tax law.

Defeasance. Unless the applicable prospectus supplement provides otherwise, the following discussion of legal defeasance and discharge and covenant defeasance will apply to any senior series of senior debt securities issued under the indentures.

Legal Defeasance. We can legally release ourselves from any payment or other obligations on the senior debt securities of any series (called "legal defeasance") if certain conditions are met, including the following:

- We deposit in trust for your benefit and the benefit of all other direct holders of the senior debt securities of the same series a combination of cash and U.S. government or U.S. government

agency obligations that will generate enough cash to make interest, principal and any other payments on the senior debt securities of that series on their various due dates.

There is a change in current U.S. federal income tax law or an IRS ruling that lets us make the above deposit without causing you to be taxed on the senior debt securities any differently than if we did not make the deposit and instead repaid the senior debt securities ourselves when due.

We deliver to the trustee a legal opinion of our counsel confirming the tax law change or ruling described above.

If we ever did accomplish legal defeasance, as described above, you would have to rely solely on the trust deposit for repayment of the debt securities. You could not look to us for repayment in the event of any shortfall.

Covenant Defeasance. Without any change of current U.S. federal tax law, we can make the same type of deposit described above and be released from some of the covenants in the senior debt securities (called "covenant defeasance"). In that event, you would lose the protection of those covenants but would gain the protection of having money and securities set aside in trust to repay the senior debt securities. In order to achieve covenant defeasance, we must do the following (among other things):

We must deposit in trust for your benefit and the benefit of all other direct holders of the senior debt securities of the same series a combination of cash and U.S. government or U.S. government agency obligations that will generate enough cash to make interest, principal and any other payments on the senior debt securities of that series on their various due dates.

We must deliver to the trustee a legal opinion of our counsel confirming that under current U.S. federal income tax law we may make the above deposit without causing you to be taxed on the senior debt securities any differently than if we did not make the deposit and instead repaid the senior debt securities ourselves when due.

If we accomplish covenant defeasance, you can still look to us for repayment of the senior debt securities if there were a shortfall in the trust deposit. In fact, if one of the events of default occurred (such as our bankruptcy) and the debt securities become immediately due and payable, there may be such a shortfall. Depending on the events causing the default, you may not be able to obtain payment of the shortfall.

Modification and Waiver. We and the trustee may amend or supplement the senior indenture or the senior debt securities without the consent of any holder:

to comply with the requirements of the SEC in order to effect or maintain the qualification of the indenture under the Trust Indenture Act of 1939, as amended, or the Trust Indenture Act;

to convey, transfer, assign, mortgage or pledge any assets as security for the senior debt securities of one or more series;

to evidence the succession of a corporation, limited liability company, partnership or trust to us, and the assumption by such successor of our covenants, agreements and obligations under the senior indenture;

to add to our covenants such new covenants, restrictions, conditions or provisions for the protection of the holders, and to make the occurrence, or the occurrence and continuance, of a default in any such additional covenants, restrictions, conditions or provisions an event of default;

to cure any ambiguity, defect or inconsistency in the senior indenture or in any supplemental indenture or to conform the senior indenture or the senior debt securities to the description of

senior debt securities of such series set forth in this prospectus or any applicable prospectus supplement;

to provide for or add guarantors with respect to the senior debt securities of any series;

to establish the form or forms or terms of the senior debt securities as permitted by the senior indenture;

to evidence and provide for the acceptance of appointment under the senior indenture by a successor trustee, or to make such changes as shall be necessary to provide for or facilitate the administration of the trusts in the senior indenture by more than one trustee;

to add to, delete from or revise the conditions, limitations and restrictions on the authorized amount, terms, purposes of issue, authentication and delivery of any series of senior debt securities;

to make any change to the senior debt securities of any series so long as no senior debt securities of such series are outstanding; or

to make any change that does not adversely affect the rights of any holder in any material respect.

Other amendments and modifications of the senior indenture or the senior debt securities issued may be made, and our compliance with any provision of the senior indenture with respect to any series of senior debt securities may be waived, with the consent of the holders of a majority of the aggregate principal amount of the outstanding senior debt securities of all series affected by the amendment or modification (voting together as a single class); provided, however, that each affected holder must consent to any modification, amendment or waiver that:

extends the final maturity of any senior debt securities of such series;

reduces the principal amount of on any senior debt securities of such series;

reduces the rate or extends the time of payment of interest on any senior debt securities of such series;

reduces the amount payable upon the redemption of any senior debt securities of such series;

changes the currency of payment of principal of or interest on any senior debt securities of such series;

reduces the principal amount of original issue discount securities payable upon acceleration of maturity or the amount provable in bankruptcy;

waives an uncured default in the payment of principal of or interest on the senior debt securities (except in the case of a rescission of acceleration as described above);

changes the provisions relating to the waiver of past defaults or changes or impairs the right of holders to receive payment or to institute suit for the enforcement of any payment or conversion of any senior debt securities of such series on or after the due date therefor;

modifies any of the provisions of these restrictions on amendments and modifications, except to increase any required percentage or to provide that certain other provisions cannot be modified or waived without the consent of the holder of each senior debt security of such series affected by the modification; or

reduces the above-stated percentage of outstanding senior debt securities of such series whose holders must consent to a supplemental indenture or to modify or amend or to waive certain provisions of or defaults under the senior indenture.

It shall not be necessary for the holders to approve the particular form of any proposed amendment, supplement or waiver, but it shall be sufficient if the holders' consent approves the substance thereof. After an amendment, supplement or waiver of the senior indenture in accordance with the provisions described in this section becomes effective, the trustee must give to the holders affected thereby certain notice briefly describing the amendment, supplement or waiver. Any failure by the trustee to give such notice, or any defect therein, shall not, however, in any way impair or affect the validity of any such amendment, supplemental indenture or waiver.

No Personal Liability of Incorporators, Stockholders, Officers, Directors. The senior indenture provides that no recourse shall be had under any obligation, covenant or agreement of ours in the senior indenture or any supplemental indenture, or in any of the senior debt securities or because of the creation of any indebtedness represented thereby, against any of our incorporators, stockholders, officers or directors, past, present or future, or of any predecessor or successor entity thereof under any law, statute or constitutional provision or by the enforcement of any assessment or by any legal or equitable proceeding or otherwise. Each holder, by accepting the senior debt securities, waives and releases all such liability.

Concerning the Trustee. The senior indenture provides that, except during the continuance of an event of default, the trustee will not be liable except for the performance of such duties as are specifically set forth in the senior indenture. If an event of default has occurred and is continuing, the trustee will exercise such rights and powers vested in it under the senior indenture and will use the same degree of care and skill in its exercise as a prudent person would exercise under the circumstances in the conduct of such person's own affairs.

The senior indenture and the provisions of the Trust Indenture Act incorporated by reference therein contain limitations on the rights of the trustee thereunder, should it become a creditor of ours or any of our subsidiaries, to obtain payment of claims in certain cases or to realize on certain property received by it in respect of any such claims, as security or otherwise. The trustee is permitted to engage in other transactions, provided that if it acquires any conflicting interest (as defined in the Trust Indenture Act), it must eliminate such conflict or resign.

We may have normal banking relationships with the senior trustee in the ordinary course of business.

Unclaimed Funds. All funds deposited with the trustee or any paying agent for the payment of principal, premium, interest or additional amounts in respect of the senior debt securities that remain unclaimed for two years after the date upon which such principal, premium or interest became due and payable will be repaid to us. Thereafter, any right of any holder of senior debt securities to such funds shall be enforceable only against us, and the trustee and paying agents will have no liability therefor.

Governing Law. The senior indenture and the senior debt securities will be governed by, and construed in accordance with, the internal laws of the State of New York.

Certain Terms of the Subordinated Debt Securities

Other than the terms of the subordinated indenture and subordinated debt securities relating to subordination or otherwise as described in the prospectus supplement relating to a particular series of subordinated debt securities, the terms of the subordinated indenture and subordinated debt securities are identical in all material respects to the terms of the senior indenture and senior debt securities.

Additional or different subordination terms may be specified in the prospectus supplement applicable to a particular series.

Subordination. The indebtedness evidenced by the subordinated debt securities is subordinate to the prior payment in full of all of our senior indebtedness, as defined in the subordinated indenture.

During the continuance beyond any applicable grace period of any default in the payment of principal, premium, interest or any other payment due on any of our senior indebtedness, we may not make any payment of principal of or interest on the subordinated debt securities (except for certain sinking fund payments). In addition, upon any payment or distribution of our assets upon any dissolution, winding-up, liquidation or reorganization, the payment of the principal of and interest on the subordinated debt securities will be subordinated to the extent provided in the subordinated indenture in right of payment to the prior payment in full of all our senior indebtedness. Because of this subordination, if we dissolve or otherwise liquidate, holders of our subordinated debt securities may receive less, ratably, than holders of our senior indebtedness. The subordination provisions do not prevent the occurrence of an event of default under the subordinated indenture.

The term "senior indebtedness" of a person means with respect to such person the principal of, premium, if any, interest on, and any other payment due pursuant to any of the following, whether outstanding on the date of the subordinated indenture or incurred by that person in the future:

- all of the indebtedness of that person for money borrowed;

- all of the indebtedness of that person evidenced by notes, debentures, bonds or other securities sold by that person for money;

- all of the lease obligations which are capitalized on the books of that person in accordance with generally accepted accounting principles;

- all indebtedness of others of the kinds described in the first two bullet points above and all lease obligations of others of the kind described in the third bullet point above that the person, in any manner, assumes or guarantees or that the person in effect guarantees through an agreement to purchase, whether that agreement is contingent or otherwise; and all renewals, extensions or refundings of indebtedness of the kinds described in the first, second or fourth bullet point above and all renewals or extensions of leases of the kinds described in the third or fourth bullet point above; unless, in the case of any particular indebtedness, renewal, extension or refunding, the instrument creating or evidencing it or the assumption or guarantee relating to it expressly provides that such indebtedness, renewal, extension or refunding is not superior in right of payment to the subordinated debt securities. Our senior debt securities constitute senior indebtedness for purposes of the subordinated debt indenture.

DESCRIPTION OF CAPITAL STOCK

The following description of our capital stock is intended as a summary only. This description is based upon, and is qualified by reference to, our restated certificate of incorporation, our amended and restated bylaws and applicable provisions of Delaware corporate law. This summary is not complete. You should read our restated certificate of incorporation and amended and restated bylaws, which are filed as exhibits to the registration statement of which this prospectus forms a part, for the provisions that are important to you.

Our authorized capital stock consists of 125,000,000 shares of common stock and 5,000,000 shares of preferred stock. As of August 23, 2017, there were 41,389,046 shares of common stock outstanding and no shares of preferred stock 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 and do not have cumulative voting rights. Each election of directors by our stockholders will be determined by a plurality of the votes cast by the stockholders entitled to vote on the election. In general, except (1) for the election of directors, (2) as described below under " Provisions of Our Certificate of Incorporation and Bylaws and Delaware Law That May Have Anti-Takeover Effects Super-Majority Voting," (3) in the future to the extent that we have two or more classes or series of stock outstanding with separate voting rights and (4) as otherwise required by law, any matter to be voted on by our stockholders at any meeting is decided by the vote of the holders of a majority in voting power of the votes cast by the holders of shares of our stock present or represented at the meeting and voting affirmatively or negatively on such matter.

Dividends. Holders of common stock are entitled to receive proportionately any dividends as may be declared by our board of directors, subject to any preferential dividend rights of outstanding preferred stock.

Liquidation and Dissolution. In the event of our liquidation or dissolution, the holders of our common stock are entitled to receive proportionately all assets available for distribution to stockholders after the payment of all debts and other liabilities and subject to the prior rights of any of our outstanding preferred stock.

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

Transfer Agent and Registrar. American Stock Transfer & Trust Company, LLC is the transfer agent and registrar for our common stock.

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

Preferred Stock

Under the terms of our certificate of incorporation, our board of directors is authorized to issue shares of preferred stock in one or more series without stockholder approval, subject to any limitations imposed by the NASDAQ Marketplace Rules. Our board of directors has the discretion to determine the rights, preferences, privileges and restrictions, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences, of each series of preferred stock. The purpose of authorizing our board of directors to issue preferred stock and determine its rights and preferences is to eliminate delays associated with a stockholder vote on specific issuances. The issuance of preferred

stock, while providing flexibility in connection with possible acquisitions, future financings and other corporate purposes, could have the effect of making it more difficult for a third party to acquire, or could discourage a third party from seeking to acquire, a majority of our outstanding voting stock. Currently, we have no shares of preferred stock outstanding.

If we decide to issue any preferred stock pursuant to this prospectus, we will describe in a prospectus supplement the specific terms of the preferred stock, including, if applicable, the following:

- 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 and, if cumulative, the date from which dividends will accumulate;
- the relative ranking and preference of the preferred stock as to dividend rights and rights if we liquidate, dissolve or wind up our affairs;
- the procedures for any auction and remarketing;
- the provisions for a sinking fund;
- the provisions for redemption or repurchase and any restrictions on our ability to exercise those redemption and repurchase rights;
- the listing of the preferred stock on any securities exchange or market;
- whether the preferred stock will be convertible into our common stock and, if convertible, 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 exchangeable, 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 any material U.S. federal income tax considerations applicable to the preferred stock;

any limitations on 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.

The preferred stock could have other rights, including economic rights that are senior to our common stock that could adversely affect the market value of our common stock. The issuance of the preferred stock may also have the effect of delaying, deferring or preventing a change in control of us without any action by the shareholders.

Stock Options and Warrants

As of June 30, 2017, we had issued and outstanding options to purchase 7,124,052 shares of our common stock at a weighted average exercise price of $29.33 per share and warrants to purchase (i) 7,030 shares of our common stock at an exercise price of $128.00 per share and (ii) 130 shares of our common stock at an exercise price of $2,520.00 per share.

Convertible Notes

In August 2015, we issued, at par value, $150.0 million aggregate principal amount of 3.0% convertible senior notes due 2022, or Convertible Notes. The Convertible Notes bear cash interest at a rate of 3.0% per year, payable semi-annually on February 15 and August 15 of each year, beginning on February 15, 2016. The Convertible Notes will mature on August 15, 2022, unless earlier repurchased or converted. The conversion rate for the Convertible Notes was initially, and remains, 17.7487 shares of our common stock per $1,000 principal amount of the Convertible Notes, which is equivalent to an initial conversion price of approximately $56.34 per share of our common stock.

Effects of Authorized but Unissued Stock

We have shares of common stock and preferred stock available for future issuance without stockholder approval, subject to any limitations imposed by the listing standards of The NASDAQ Global Select Market. We may utilize these additional shares for a variety of corporate purposes, including for future public offerings to raise additional capital or facilitate corporate acquisitions or for payment as a dividend on our capital stock. The existence of unissued and unreserved common stock and preferred stock may enable our board of directors to issue shares to persons friendly to current management or to issue preferred stock with terms that could have the effect of making it more difficult for a third party to acquire, or could discourage a third party from seeking to acquire, a controlling interest in our company by means of a merger, tender offer, proxy contest or otherwise. In addition, if we issue preferred stock, the issuance could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive dividend payments and payments upon liquidation.

Provisions of Our Certificate of Incorporation and Bylaws and Delaware Law That May Have Anti-Takeover Effects

Delaware Law. We are subject to Section 203 of the Delaware General Corporation Law. Subject to certain exceptions, Section 203 prevents a publicly held Delaware corporation from engaging in a "business combination" with any "interested stockholder" for three years following the date that the person became an interested stockholder, unless either the interested stockholder attained such status with the approval of our board of directors, the business combination is approved by our board of directors and stockholders in a prescribed manner or the interested stockholder acquired at least 85% of our outstanding voting stock in the transaction in which it became an interested stockholder. A "business combination" includes, among other things, a merger or consolidation involving us and the "interested stockholder" and the sale of more than 10% of our assets. In general, an "interested stockholder" is any entity or person beneficially owning 15% or more of our outstanding voting stock and any entity or person affiliated with or controlling or controlled by such entity or person. The restrictions contained in Section 203 are not applicable to any of our existing stockholders that owned 15% or more of our outstanding voting stock upon the closing of our initial public offering.

Staggered Board; Removal of Directors. Our certificate of incorporation and our bylaws divide our board of directors into three classes with staggered three-year terms. In addition, our certificate of incorporation and our bylaws provide that directors may be removed only for cause and only by the affirmative vote of the holders of 75% of our shares of capital stock present in person or by proxy and entitled to vote. Under our certificate of incorporation and bylaws, any vacancy on our board of directors,

including a vacancy resulting from an enlargement of our board of directors, may be filled only by vote of a majority of our directors then in office. Furthermore, our certificate of incorporation provides that the authorized number of directors may be changed only by the resolution of our board of directors. The classification of our board of directors and the limitations on the ability of our stockholders to remove directors, change the authorized number of directors and fill vacancies could make it more difficult for a third party to acquire, or discourage a third party from seeking to acquire, control of our company.

Stockholder Action; Special Meeting of Stockholders; Advance Notice Requirements for Stockholder Proposals and Director Nominations. Our certificate of incorporation and our bylaws provide that any action required or permitted to be taken by our stockholders at an annual meeting or special meeting of stockholders may only be taken if it is properly brought before such meeting and may not be taken by written action in lieu of a meeting. Our certificate of incorporation and our bylaws also provide that, except as otherwise required by law, special meetings of the stockholders can only be called by our chairman of the board, our president or chief executive officer or our board of directors. In addition, our bylaws establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of stockholders, including proposed nominations of candidates for election to our board of directors. Stockholders at an annual meeting may only consider proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of our board of directors, or by a stockholder of record on the record date for the meeting, who is entitled to vote at the meeting and who has delivered timely written notice in proper form to our secretary of the stockholder's intention to bring such business before the meeting. These provisions could have the effect of delaying until the next stockholder meeting stockholder actions that are favored by the holders of a majority of our outstanding voting securities. These provisions also could discourage a third party from making a tender offer for our common stock, because even if it acquired a majority of our outstanding voting stock, it would be able to take action as a stockholder, such as electing new directors or approving a merger, only at a duly called stockholders meeting and not by written consent.

Super-Majority Voting. The Delaware General Corporation Law provides generally that the affirmative vote of a majority of the shares entitled to vote on any matter is required to amend a corporation's certificate of incorporation or bylaws, unless a corporation's certificate of incorporation or bylaws, as the case may be, requires a greater percentage. Our bylaws may be amended or repealed by a majority vote of our board of directors or the affirmative vote of the holders of at least 75% of the votes that all our stockholders would be entitled to cast in any annual election of directors. In addition, the affirmative vote of the holders of at least 75% of the votes that all our stockholders would be entitled to cast in any election of directors is required to amend or repeal or to adopt any provisions inconsistent with any of the provisions of our certificate of incorporation described above.

Directors' Liability

Our certificate of incorporation limits the personal liability of directors for breach of fiduciary duty to the maximum extent permitted by the Delaware General Corporation Law and provides that no director will have personal liability to us or to our stockholders for monetary damages for breach of fiduciary duty or other duty as a director. However, these provisions do not eliminate or limit the liability of any of our directors:

for any breach of the director's duty of loyalty to us or our stockholders;

for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law;

for voting or assenting to unlawful payments of dividends, stock repurchases or other distributions; or

for any transaction from which the director derived an improper personal benefit.

Any amendment to or repeal of these provisions will not eliminate or reduce the effect of these provisions in respect of any act, omission or claim that occurred or arose prior to such amendment or repeal. If the Delaware General Corporation Law is amended to provide for further limitations on the personal liability of directors of corporations, then the personal liability of our directors will be further limited to the greatest extent permitted by the Delaware General Corporation Law.

In addition, our certificate of incorporation provides that we must indemnify our directors and officers and we must advance expenses, including attorneys' fees, to our directors and officers in connection with legal proceedings, subject to very limited exceptions.

We maintain a general liability insurance policy that covers certain liabilities of our directors and officers arising out of claims based on acts or omissions in their capacities as directors or officers. In addition, we have entered into indemnification agreements with our directors. These indemnification agreements may require us, among other things, to indemnify each such director for some expenses, including attorneys' fees, judgments, fines and settlement amounts incurred by him in any action or proceeding arising out of his service as one of our directors.

Certain of our non-employee directors may, through their relationships with their employers, be insured and/or indemnified against certain liabilities incurred in their capacity as members of our board of directors.

DESCRIPTION OF DEPOSITARY SHARES

General

We may, at our option, elect to offer fractional shares of preferred stock, which we call depositary shares, rather than full shares of preferred stock. If we do, we will issue to the public receipts, called depositary receipts, for depositary shares, each of which will represent a fraction, to be described in the applicable prospectus supplement, of a share of a particular series of preferred stock. Unless otherwise provided in the prospectus supplement, each owner of a depositary share will be entitled, in proportion to the applicable fractional interest in a share of preferred stock represented by the depositary share, to all the rights and preferences of the preferred stock represented by the depositary share. Those rights include dividend, voting, redemption, conversion and liquidation rights.

The shares of preferred stock underlying the depositary shares will be deposited with a bank or trust company selected by us to act as depositary under a deposit agreement between us, the depositary and the holders of the depositary receipts. The depositary will be the transfer agent, registrar and dividend disbursing agent for the depositary shares.

The depositary shares will be evidenced by depositary receipts issued pursuant to the deposit agreement. Holders of depositary receipts agree to be bound by the deposit agreement, which requires holders to take certain actions such as filing proof of residence and paying certain charges.

The summary of terms of the depositary shares contained in this prospectus is not complete. You should refer to the form of the deposit agreement, our certificate of incorporation and the certificate of designation for the applicable series of preferred stock that are, or will be, filed with the SEC.

Dividends and Other Distributions

The depositary will distribute all cash dividends or other cash distributions, if any, received in respect of the preferred stock underlying the depositary shares to the record holders of depositary shares in proportion to the numbers of depositary shares owned by those holders on the relevant record date. The relevant record date for depositary shares will be the same date as the record date for the underlying preferred stock.

If there is a distribution other than in cash, the depositary will distribute property (including securities) received by it to the record holders of depositary shares, unless the depositary determines that it is not feasible to make the distribution. If this occurs, the depositary may, with our approval, adopt another method for the distribution, including selling the property and distributing the net proceeds from the sale to the holders.

Liquidation Preference

If a series of preferred stock underlying the depositary shares has a liquidation preference, in the event of the voluntary or involuntary liquidation, dissolution or winding up of us, holders of depositary shares will be entitled to receive the fraction of the liquidation preference accorded each share of the applicable series of preferred stock, as set forth in the applicable prospectus supplement.

Withdrawal of Stock

Unless the related depositary shares have been previously called for redemption, upon surrender of the depositary receipts at the office of the depositary, the holder of the depositary shares will be entitled to delivery, at the office of the depositary to or upon his or her order, of the number of whole shares of the preferred stock and any money or other property represented by the depositary shares. If the depositary receipts delivered by the holder evidence a number of depositary shares in excess of the number of depositary shares representing the number of whole shares of preferred stock to be

withdrawn, the depositary will deliver to the holder at the same time a new depositary receipt evidencing the excess number of depositary shares. In no event will the depositary deliver fractional shares of preferred stock upon surrender of depositary receipts. Holders of preferred stock thus withdrawn may not thereafter deposit those shares under the deposit agreement or receive depositary receipts evidencing depositary shares therefor.

Redemption of Depositary Shares

Whenever we redeem shares of preferred stock held by the depositary, the depositary will redeem as of the same redemption date the number of depositary shares representing shares of the preferred stock so redeemed, so long as we have paid in full to the depositary the redemption price of the preferred stock to be redeemed plus an amount equal to any accumulated and unpaid dividends on the preferred stock to the date fixed for redemption. The redemption price per depositary share will be equal to the redemption price and any other amounts per share payable on the preferred stock multiplied by the fraction of a share of preferred stock represented by one depositary share. If less than all the depositary shares are to be redeemed, the depositary shares to be redeemed will be selected by lot or pro rata or by any other equitable method as may be determined by the depositary.

After the date fixed for redemption, depositary shares called for redemption will no longer be deemed to be outstanding and all rights of the holders of depositary shares will cease, except the right to receive the monies payable upon redemption and any money or other property to which the holders of the depositary shares were entitled upon redemption upon surrender to the depositary of the depositary receipts evidencing the depositary shares.

Voting the Preferred Stock

Upon receipt of notice of any meeting at which the holders of the preferred stock are entitled to vote, the depositary will mail the information contained in the notice of meeting to the record holders of the depositary receipts relating to that preferred stock. The record date for the depositary receipts relating to the preferred stock will be the same date as the record date for the preferred stock. Each record holder of the depositary shares on the record date will be entitled to instruct the depositary as to the exercise of the voting rights pertaining to the number of shares of preferred stock represented by that holder's depositary shares. The depositary will endeavor, insofar as practicable, to vote the number of shares of preferred stock represented by the depositary shares in accordance with those instructions, and we will agree to take all action that may be deemed necessary by the depositary in order to enable the depositary to do so. The depositary will not vote any shares of preferred stock except to the extent it receives specific instructions from the holders of depositary shares representing that number of shares of preferred stock.

Charges of Depositary

We will pay all transfer and other taxes and governmental charges arising solely from the existence of the depositary arrangements. We will pay charges of the depositary in connection with the initial deposit of the preferred stock and any redemption of the preferred stock. Holders of depositary receipts will pay transfer, income and other taxes and governmental charges and such other charges (including those in connection with the receipt and distribution of dividends, the sale or exercise of rights, the withdrawal of the preferred stock and the transferring, splitting or grouping of depositary receipts) as are expressly provided in the deposit agreement to be for their accounts. If these charges have not been paid by the holders of depositary receipts, the depositary may refuse to transfer depositary shares, withhold dividends and distributions and sell the depositary shares evidenced by the depositary receipt.

Amendment and Termination of the Deposit Agreement

The form of depositary receipt evidencing the depositary shares and any provision of the deposit agreement may be amended by agreement between us and the depositary. However, any amendment that materially and adversely alters the rights of the holders of depositary shares, other than fee changes, will not be effective unless the amendment has been approved by the holders of a majority of the outstanding depositary shares. The deposit agreement may be terminated by the depositary or us only if:

all outstanding depositary shares have been redeemed; or

there has been a final distribution of the preferred stock in connection with our dissolution and such distribution has been made to all the holders of depositary shares.

Resignation and Removal of Depositary

The depositary may resign at any time by delivering to us notice of its election to do so, and we may remove the depositary at any time. Any resignation or removal of the depositary will take effect upon our appointment of a successor depositary and its acceptance of such appointment. The successor depositary must be appointed within 60 days after delivery of the notice of resignation or removal and must be a bank or trust company having its principal office in the United States and having the requisite combined capital and surplus as set forth in the applicable agreement.

Notices

The depositary will forward to holders of depositary receipts all notices, reports and other communications, including proxy solicitation materials received from us, that are delivered to the depositary and that we are required to furnish to the holders of the preferred stock. In addition, the depositary will make available for inspection by holders of depositary receipts at the principal office of the depositary, and at such other places as it may from time to time deem advisable, any reports and communications we deliver to the depositary as the holder of preferred stock.

Limitation of Liability

Neither we nor the depositary will be liable if either is prevented or delayed by law or any circumstance beyond its control in performing its obligations. Our obligations and those of the depositary will be limited to performance in good faith of our and their duties thereunder. We and the depositary will not be obligated to prosecute or defend any legal proceeding in respect of any depositary shares or preferred stock unless satisfactory indemnity is furnished. We and the depositary may rely upon written advice of counsel or accountants, on information provided by persons presenting preferred stock for deposit, holders of depositary receipts or other persons believed to be competent to give such information and on documents believed to be genuine and to have been signed or presented by the proper party or parties.

DESCRIPTION OF PURCHASE CONTRACTS AND PURCHASE UNITS

We may issue purchase contracts, including contracts obligating holders to purchase from or sell to us, and obligating us to sell to or purchase from the holders, a specified number of shares of our common stock, preferred stock or depositary shares at a future date or dates, which we refer to in this prospectus as purchase contracts. The price per share of common stock, preferred stock or depositary shares and the number of shares of each may be fixed at the time the purchase contracts are issued or may be determined by reference to a specific formula set forth in the purchase contracts. The purchase contracts may be issued separately or as part of units, often known as purchase units, consisting of one or more purchase contracts and beneficial interests in debt securities or any other securities described in the applicable prospectus supplement or any combination of the foregoing, securing the holders' obligations to purchase the common stock, preferred stock or depositary shares under the purchase contracts.

The purchase contracts may require us to make periodic payments to the holders of the purchase units or vice versa, and these payments may be unsecured or prefunded on some basis. The purchase contracts may require holders to secure their obligations under those contracts in a specified manner, including pledging their interest in another purchase contract.

The applicable prospectus supplement will describe the terms of the purchase contracts and purchase units, including, if applicable, collateral or depositary arrangements.

DESCRIPTION OF WARRANTS

We may issue warrants to purchase debt securities, common stock, preferred stock or depositary shares. We may offer warrants separately or together with one or more additional warrants, debt securities, common stock, preferred stock or depositary shares, or any combination of those securities in the form of units, as described in the applicable prospectus supplement. If we issue warrants as part of a unit, the accompanying prospectus supplement will specify whether those warrants may be separated from the other securities in the unit prior to the expiration date of the warrants. The applicable prospectus supplement will also describe the following terms of any warrants:

the specific designation and aggregate number of, and the offering price at which we will issue, the warrants;

the currency or currency units in which the offering price, if any, and the exercise price are payable;

the date on which the right to exercise the warrants will begin and the date on which that right will expire or, if you may not continuously exercise the warrants throughout that period, the specific date or dates on which you may exercise the warrants;

whether the warrants are to be sold separately or with other securities as parts of units;

whether the warrants will be issued in definitive or global form or in any combination of these forms, although, in any case, the form of a warrant included in a unit will correspond to the form of the unit and of any security included in that unit;

any applicable material U.S. federal income tax consequences;

the identity of the warrant agent for the warrants and of any other depositaries, execution or paying agents, transfer agents, registrars or other agents;

the proposed listing, if any, of the warrants or any securities purchasable upon exercise of the warrants on any securities exchange;

the designation and terms of any equity securities purchasable upon exercise of the warrants;

the designation, aggregate principal amount, currency and terms of any debt securities that may be purchased upon exercise of the warrants;

if applicable, the designation and terms of the debt securities, common stock, preferred stock or depositary shares with which the warrants are issued and, the number of warrants issued with each security;

if applicable, the date from and after which any warrants issued as part of a unit and the related debt securities, common stock, preferred stock or depositary shares will be separately transferable;

the number of shares of common stock, the number of shares of preferred stock or the number of depositary shares purchasable upon exercise of a warrant and the price at which those shares may be purchased;

if applicable, the minimum or maximum amount of the warrants that may be exercised at any one time;

information with respect to book-entry procedures, if any;

the antidilution provisions of, and other provisions for changes to or adjustment in the exercise price of, the warrants, if any;

any redemption or call provisions; and

any additional terms of the warrants, including terms, procedures and limitations relating to the exchange or exercise of the warrants.

FORMS OF SECURITIES

Each debt security, depositary share, purchase contract, purchase unit and warrant will be represented either by a certificate issued in definitive form to a particular investor or by one or more global securities representing the entire issuance of securities. Unless the applicable prospectus supplement provides otherwise, certificated securities will be issued in definitive form and global securities will be issued in registered form. Definitive securities name you or your nominee as the owner of the security, and in order to transfer or exchange these securities or to receive payments other than interest or other interim payments, you or your nominee must physically deliver the securities to the trustee, registrar, paying agent or other agent, as applicable. Global securities name a depositary or its nominee as the owner of the debt securities, depositary shares, purchase contracts, purchase units or warrants represented by these global securities. The depositary maintains a computerized system that will reflect each investor's beneficial ownership of the securities through an account maintained by the investor with its broker/dealer, bank, trust company or other representative, as we explain more fully below.

Registered Global Securities

We may issue the registered debt securities, depositary shares, purchase contracts, purchase units and warrants in the form of one or more fully registered global securities that will be deposited with a depositary or its nominee identified in the applicable prospectus supplement and registered in the name of that depositary or nominee. In those cases, one or more registered global securities will be issued in a denomination or aggregate denominations equal to the portion of the aggregate principal or face amount of the securities to be represented by registered global securities. Unless and until it is exchanged in whole for securities in definitive registered form, a registered global security may not be transferred except as a whole by and among the depositary for the registered global security, the nominees of the depositary or any successors of the depositary or those nominees.

If not described below, any specific terms of the depositary arrangement with respect to any securities to be represented by a registered global security will be described in the prospectus supplement relating to those securities. We anticipate that the following provisions will apply to all depositary arrangements.

Ownership of beneficial interests in a registered global security will be limited to persons, called participants, that have accounts with the depositary or persons that may hold interests through participants. Upon the issuance of a registered global security, the depositary will credit, on its book-entry registration and transfer system, the participants' accounts with the respective principal or face amounts of the securities beneficially owned by the participants. Any dealers, underwriters or agents participating in the distribution of the securities will designate the accounts to be credited. Ownership of beneficial interests in a registered global security will be shown on, and the transfer of ownership interests will be effected only through, records maintained by the depositary, with respect to interests of participants, and on the records of participants, with respect to interests of persons holding through participants. The laws of some states may require that some purchasers of securities take physical delivery of these securities in definitive form. These laws may impair your ability to own, transfer or pledge beneficial interests in registered global securities.

So long as the depositary, or its nominee, is the registered owner of a registered global security, that depositary or its nominee, as the case may be, will be considered the sole owner or holder of the securities represented by the registered global security for all purposes under the applicable indenture, deposit agreement, purchase contract, warrant agreement or purchase unit agreement. Except as described below, owners of beneficial interests in a registered global security will not be entitled to have the securities represented by the registered global security registered in their names, will not receive or be entitled to receive physical delivery of the securities in definitive form and will not be

considered the owners or holders of the securities under the applicable indenture, deposit agreement, purchase contract, purchase unit agreement or warrant agreement. Accordingly, each person owning a beneficial interest in a registered global security must rely on the procedures of the depositary for that registered global security and, if that person is not a participant, on the procedures of the participant through which the person owns its interest, to exercise any rights of a holder under the applicable indenture, deposit agreement, purchase contract, purchase unit agreement or warrant agreement. We understand that under existing industry practices, if we request any action of holders or if an owner of a beneficial interest in a registered global security desires to give or take any action that a holder is entitled to give or take under the applicable indenture, deposit agreement, purchase contract, purchase unit agreement or warrant agreement, the depositary for the registered global security would authorize the participants holding the relevant beneficial interests to give or take that action, and the participants would authorize beneficial owners owning through them to give or take that action or would otherwise act upon the instructions of beneficial owners holding through them.

Principal, premium, if any, and interest payments on debt securities, and any payments to holders with respect to depositary shares, warrants, purchase agreements or purchase units, represented by a registered global security registered in the name of a depositary or its nominee will be made to the depositary or its nominee, as the case may be, as the registered owner of the registered global security. None of us, the trustees, the warrant agents, the unit agents or any other agent of ours, agent of the trustees or agent of the warrant agents or unit agents will have any responsibility or liability for any aspect of the records relating to payments made on account of beneficial ownership interests in the registered global security or for maintaining, supervising or reviewing any records relating to those beneficial ownership interests.

We expect that the depositary for any of the securities represented by a registered global security, upon receipt of any payment to holders of principal, premium, interest or other distribution of underlying securities or other property on that registered global security, will immediately credit participants' accounts in amounts proportionate to their respective beneficial interests in that registered global security as shown on the records of the depositary. We also expect that payments by participants to owners of beneficial interests in a registered global security held through participants will be governed by standing customer instructions and customary practices, as is now the case with the securities held for the accounts of customers or registered in "street name," and will be the responsibility of those participants.

If the depositary for any of the securities represented by a registered global security is at any time unwilling or unable to continue as depositary or ceases to be a clearing agency registered under the Exchange Act, and a successor depositary registered as a clearing agency under the Exchange Act is not appointed by us within 90 days, we will issue securities in definitive form in exchange for the registered global security that had been held by the depositary. Any securities issued in definitive form in exchange for a registered global security will be registered in the name or names that the depositary gives to the relevant trustee, warrant agent, unit agent or other relevant agent of ours or theirs. It is expected that the depositary's instructions will be based upon directions received by the depositary from participants with respect to ownership of beneficial interests in the registered global security that had been held by the depositary.

PLAN OF DISTRIBUTION

We or a selling stockholder may sell securities:

- to or through underwriters, brokers or dealers;
- through agents;
- directly to one or more other purchasers in negotiated sales or competitively bid transactions;
- through a block trade in which the broker or dealer engaged to handle the block trade will attempt to sell the securities as agent, but may position and resell a portion of the block as principal to facilitate the transaction; or
- through a combination of any of the above methods of sale.

In addition, we may issue the securities as a dividend or distribution or in a subscription rights offering to our existing security holders.

We or any selling stockholder may directly solicit offers to purchase securities, or agents may be designated to solicit such offers. We will, in the prospectus supplement relating to such offering, name any agent that could be viewed as an underwriter under the Securities Act, and describe any commissions that we must pay. Any such agent will be acting on a best efforts basis for the period of its appointment or, if indicated in the applicable prospectus supplement, on a firm commitment basis. This prospectus may be used in connection with any offering of our securities through any of these methods or other methods described in the applicable prospectus supplement.

The distribution of the securities may be effected 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 such prevailing market prices; or
- at negotiated prices.

Each prospectus supplement will describe the method of distribution of the securities and any applicable restrictions.

The prospectus supplement with respect to the securities of a particular series will describe the terms of the offering of the securities, including the following:

- the name of the agent or any underwriters;
- the public offering or purchase price;
- and the proceeds we will receive from the sales of securities;

any discounts and commissions to be allowed or paid to the agent or underwriters;

all other items constituting underwriting compensation;

any discounts and commissions to be allowed or re-allowed or paid to dealers; and

any exchanges on which the securities will be listed.

If any underwriters or agents are utilized in the sale of the securities in respect of which this prospectus is delivered, we will enter into an underwriting agreement or other agreement with them at the time of sale to them, and we will set forth in the prospectus supplement relating to such offering the names of the underwriters or agents and the terms of the related agreement with them.

If a dealer is utilized in the sale of the securities in respect of which the prospectus is delivered, we or a selling stockholder will sell such securities to the dealer, as principal. The dealer may then resell such securities to the public at varying prices to be determined by such dealer at the time of resale.

If we offer securities in a subscription rights offering to our existing security holders, we may enter into a standby underwriting agreement with dealers, acting as standby underwriters. We may pay the standby underwriters a commitment fee for the securities they commit to purchase on a standby basis. If we do not enter into a standby underwriting arrangement, we may retain a dealer-manager to manage a subscription rights offering for us.

Remarketing firms, agents, underwriters, dealers and other persons may be entitled under agreements which they may enter into with us to indemnification by us against certain civil liabilities, including liabilities under the Securities Act, and may be customers of, engage in transactions with or perform services for us in the ordinary course of business.

We may pay expenses incurred with respect to the registration of the shares of common stock owned by any selling stockholders.

If so indicated in the applicable prospectus supplement, we or any selling stockholder will authorize underwriters or other persons acting as our agents to solicit offers by certain institutions to purchase securities from us pursuant to delayed delivery contracts providing for payment and delivery on the date stated in the prospectus supplement. Each contract will be for an amount not less than, and the aggregate amount of securities sold pursuant to such contracts shall not be less nor more than, the respective amounts stated in the prospectus supplement. Institutions with whom the contracts, when authorized, may be made include commercial and savings banks, insurance companies, pension funds, investment companies, educational and charitable institutions and other institutions, but shall in all cases be subject to our approval. Delayed delivery contracts will not be subject to any conditions except that:

- the purchase by an institution of the securities covered under that contract shall not at the time of delivery be prohibited under the laws of the jurisdiction to which that institution is subject; and

- if the securities are also being sold to underwriters acting as principals for their own account, the underwriters shall have purchased such securities not sold for delayed delivery. The underwriters and other persons acting as our agents will not have any responsibility in respect of the validity or performance of delayed delivery contracts.

Certain agents, underwriters and dealers, and their associates and affiliates may be customers of, have borrowing relationships with, engage in other transactions with, or perform services, including investment banking services, for us or one or more of our respective affiliates or any selling stockholder in the ordinary course of business.

In order to facilitate the offering of the securities, any underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of the securities or any other securities the prices of which may be used to determine payments on such securities. Specifically, any underwriters may overallot in connection with the offering, creating a short position for their own accounts. In addition, to cover overallotments or to stabilize the price of the securities or of any such other securities, the underwriters may bid for, and purchase, the securities or any such other securities in the open market. Finally, in any offering of the securities through a syndicate of underwriters, the underwriting syndicate may reclaim selling concessions allowed to an underwriter or a dealer for distributing the securities in the offering if the syndicate repurchases previously distributed securities in transactions to cover syndicate short positions, in stabilization transactions or otherwise. Any of these activities may stabilize

or maintain the market price of the securities above independent market levels. Any such underwriters are not required to engage in these activities and may end any of these activities at any time.

Under Rule 15c6-1 of the Exchange Act, trades in the secondary market generally are required to settle in two business days, unless the parties to any such trade expressly agree otherwise. The applicable prospectus supplement may provide that the original issue date for your securities may be more than two scheduled business days after the trade date for your securities. Accordingly, in such a case, if you wish to trade securities on any date prior to the second business day before the original issue date for your securities, you will be required, by virtue of the fact that your securities initially are expected to settle in more than two scheduled business days after the trade date for your securities, to make alternative settlement arrangements to prevent a failed settlement.

To comply with the securities laws of some states, if applicable, the securities may be sold in such jurisdictions only through registered or licensed brokers or dealers. In addition, in some states the securities may not be sold unless they have been registered or qualified for sale or an exemption from registration or qualification requirements is available and is complied with.

The securities may be new issues of securities and may have no established trading market. The securities may or may not be listed on a national securities exchange. We can make no assurance as to the liquidity of or the existence of trading markets for any of the securities.

LEGAL MATTERS

Unless the applicable prospectus supplement indicates otherwise, the validity of the securities in respect of which this prospectus is being delivered will be passed upon by Wilmer Cutler Pickering Hale and Dorr LLP.

EXPERTS

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

The financial statements of the Emflaza Business as of and for the years ended December 31, 2016 and 2015, incorporated in this prospectus by reference from the Current Report on Form 8-K/A dated July 3, 2017 of PTC Therapeutics, Inc, have been audited by Deloitte & Touche LLP, independent auditors, as stated in their report (which report expresses an unmodified opinion and includes an emphasis-of-matter paragraph relating to the allocation of certain assets, liabilities, expenses, and income that have historically been held at the Marathon Pharmaceutical Holdings, LLC corporate level but which are specifically identifiable or attributable to the Emflaza Business), which is incorporated herein by reference. Such financial statements have been so incorporated in reliance upon the report of such firm given upon their authority as experts in accounting and auditing.

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$200 million

Common Stock

RBC Capital Markets