This prospectus is not complete and may be changed. These securities may not be sold until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell these securities and we are not soliciting offers to buy these securities in any jurisdiction where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED August 1, 2016

Preliminary Prospectus

5,835,000 Shares

Protagonist Therapeutics

Common Stock

Protagonist Therapeutics, Inc. is offering 5,835,000 shares of its common stock. This is our initial public offering, and no public market currently exists for our shares. We anticipate that the initial public offering price will be between $11.00 and $13.00 per share.

Prior to this offering, there has been no public market for our common stock. We have applied to have our common stock listed on The NASDAQ Global Market under the symbol "PTGX."

We are an "emerging growth company" as that term is used in the Jumpstart Our Business Startups Act of 2012, and, as such, have elected to comply with certain reduced public company reporting requirements.

Investing in our common stock involves a high degree of risk. Before buying any shares, you should carefully read the discussion of material risks of investing in our common stock in "Risk Factors" beginning on page 12 of this prospectus.

	Per Share	Total
Initial public offering price	$	$
Underwriting discounts and commissions[1]	$	$
Proceeds, before expenses, to us	$	$

(1) We have agreed to reimburse the underwriters for certain expenses in connection with this offering. See "Underwriting."

We have granted the underwriters an option for a period of 30 days to purchase up to 875,250 additional shares of common stock. The underwriters can exercise this right at any time within 30 days after the date of this prospectus.

Certain of our existing stockholders and their affiliated entities, including investors affiliated with certain of our directors, have indicated an interest in purchasing an aggregate of up to approximately $40.0 million in shares of our common stock in this offering at the initial public offering price and on the same terms as the other purchasers in this offering. However, because indications of interest are not binding agreements or commitments to purchase, these investors may determine to purchase fewer shares than they indicate an interest in purchasing or not to purchase any shares in this offering. It is also possible that these investors could indicate an interest in purchasing more shares of our common stock. In addition, the underwriters could determine to sell fewer shares to any of these investors than the investors indicate an interest in purchasing or not to sell any shares to these investors.

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

The underwriters expect to deliver the shares of common stock to investors on or about , 2016.

Leerink Partners **Barclays** **BMO Capital Markets**

The date of this prospectus is , 2016.


Protagonist
Therapeutics

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You should rely only on the information contained in this prospectus or in any free writing prospectus we may authorize to be delivered or made available to you. We have not authorized anyone to provide you with different information. We are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where offers and sales are permitted. The information in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or of any sale of shares of our common stock. Our business, financial condition, results of operations and prospects may have changed since that date.

For investors outside the United States: We have not, and the underwriters have not done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than in the United States. Persons outside the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of the shares of common stock and the distribution of this prospectus outside the United States.

Our name "Protagonist Therapeutics," the Protagonist Therapeutics logo and other trademarks or service marks of Protagonist Therapeutics, Inc. appearing in this prospectus are the property of Protagonist Therapeutics, Inc. This prospectus also includes trademarks, tradenames, and service marks that are the property of other organizations. Solely for convenience, trademarks and tradenames referred to in this prospectus appear without the ® and ™ symbols, but those references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or that the applicable owner will not assert its rights, to these trademarks and tradenames. We do not intend our use of display of other companies' trade names, trademarks, or service marks to imply a relationship with, or endorsement or sponsorship of us by, these other companies.

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PROSPECTUS SUMMARY

This summary highlights information contained elsewhere in this prospectus. This summary does not contain all of the information you should consider before investing in our common stock. You should read this entire prospectus carefully, including the sections in this prospectus entitled "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our consolidated financial statements and the related notes thereto included at the end of this prospectus, before making an investment decision. As used in this prospectus, unless the context otherwise requires, references to "we," "us," "our," "our company" and "Protagonist" refer to Protagonist Therapeutics, Inc.

Overview

We are a clinical-stage biopharmaceutical company with a proprietary technology platform focused on discovering and developing peptide-based new chemical entities (NCEs) to address significant unmet medical needs. Our primary focus is on developing first-in-class oral peptide drugs that specifically target biological pathways also targeted by currently marketed injectable antibody drugs. Compared to injectable antibody drugs, our oral peptides offer targeted delivery to the gastrointestinal (GI) tissue compartment, potential for improved safety due to minimal exposure in the blood, improved convenience and compliance due to oral delivery, and the opportunity for earlier introduction of targeted therapy for inflammatory bowel disease (IBD). Our initial lead product candidates, PTG-100 and PTG-200, are based on this approach, and we believe they have the potential to transform the existing treatment paradigm for IBD, a GI disease consisting primarily of ulcerative colitis (UC) and Crohn's disease (CD).

PTG-100 is a potential first-in-class oral, alpha-4-beta-7 ($\alpha4\beta7$) integrin-specific antagonist peptide product candidate which has now completed a Phase 1 clinical trial in normal healthy volunteers (NHVs). Integrins are T cell receptors that facilitate migration of inflammatory cells into the GI tissue. An integrin antagonist peptide is a small molecule designed to block this migration, which is a hallmark of IBD. In our Phase 1 clinical trial, we have established pharmacological proof-of-concept (POC) based on pharmacodynamic (PD) indicators. We plan to initiate a Phase 2b clinical trial in moderate-to-severe UC patients by the end of the fourth quarter of 2016. The $\alpha4\beta7$ integrin is targeted by currently marketed injectable antibody drugs and the integrin pathway is considered to be one of the most specific biological mechanisms for IBD. Our second product candidate, PTG-200, is a potential first-in-class oral Interleukin-23 receptor (IL-23R) antagonist being developed initially for moderate-to-severe CD. Interleukin-23 is a protein produced by white blood cells that regulates inflammatory and immune functions. PTG-200 is currently in Investigational New Drug (IND) enabling studies, and we plan to initiate a Phase 1 clinical trial in 2017.

IBD is a chronic inflammatory disease with significant unmet medical need, which has created a large and growing market with an estimated 1.6 million patients in the United States in 2013. As of 2008, annual direct treatment costs for patients with IBD in the United States were estimated to exceed $6.3 billion, with indirect costs estimated to be an additional $5.5 billion. In 2012, Global Data estimated that the UC and CD markets reached approximately $4.2 billion and $3.2 billion, respectively, across ten major markets, and Global Data estimates that these markets are expected to grow at a compound annual growth rate of approximately 3% to 5% through 2022. The current tumor necrosis factor-alpha (TNF-α) antibody drugs approved for moderate-to-severe IBD, Humira® and Remicade®, are both injectable. According to Global Data, the 2013 sales for Humira® and Remicade® for IBD were $3.4 billion in the United States. Approximately one third of IBD patients are non-responders to TNF-α antibody drugs and approximately another 30% to 40% become refractory within the first year of treatment. Additionally, TNF-α antibody drugs may predispose patients to an increased risk of serious infection and the development of anti-drug antibodies (ADAs), which over time can cause loss of drug response. Thus, while available treatments exist for moderate-to-severe IBD, there continues to be a significant medical need for efficacious, safer, and convenient treatments.

We believe PTG-100 and PTG-200 have the potential to transform the existing IBD treatment paradigm because they offer significant advantages over injectable antibody drugs. These complementary assets target different biological pathways, and potentially offer improved convenience, patient compliance, and safety and tolerability compared to currently approved injectable antibody drugs. We believe these potential advantages could allow our products to replace and expand the IBD market beyond the moderate-to-severe IBD patient population currently treated by injectable antibody drugs.

PTG-100 and PTG-200 are derived from our proprietary peptide technology platform. Peptide therapeutics represent a substantial and growing therapeutic class with more than 60 FDA approved drugs. Our platform enables us to discover novel, structurally constrained peptides that retain certain key advantages of both oral small molecule and injectable antibody drugs, while overcoming many of their limitations as therapeutics. Constrained peptides are rigid, well-folded structures typically formed by disulfide bonds that alleviate the fundamental instability inherent in traditional peptides, which cannot be delivered orally. Further, these constrained peptides are designed to bind to biological targets, including protein-protein interaction (PPI) targets, which are typically approached by antibodies since small molecules cannot bind effectively to these targets. It is estimated that up to 80% of all potential disease targets are not amenable to drug development by small molecules and have therefore traditionally been approached by injectable antibody drugs.

Our novel peptides have potential applicability in a wide range of therapeutic areas in addition to GI diseases. Our first product candidate beyond IBD is PTG-300, an injectable hepcidin mimetic, which is currently in pre-clinical development with completion of IND-enabling studies expected by the end of the first half of 2017. A hepcidin mimetic is a peptide that mimics the function of the natural hormone, hepcidin. PTG-300 has potential utility for the treatment of iron overload disorders, such as transfusion-dependent β-Thalassemia, hereditary hemochromatosis (HH) and sickle cell disease (SCD), each of which may qualify PTG-300 for orphan drug designation.

Our Pipeline

We will continue to leverage our proprietary peptide technology platform to discover and develop novel product candidates to treat diseases with significant unmet medical needs. The following table summarizes key information about our peptide product candidates to date:

			Development Status				
Program	**Dosing Form**	**Indication**	**Preclinical**	**Phase 1**	**Phase 2**	**Anticipated Milestones**	**Commercial Rights**
PTG-100 (α4β7 Antagonist)	Oral	IBD (Ulcerative Colitis)				Initiate Phase 2b Clinical Trial by the end of Q4 2016	Worldwide
PTG-200 (IL-23R Antagonist)	Oral	IBD (Crohn's Disease)				Initiate Phase 1 Clinical Trial in 2017	Worldwide
PTG-300 (Hepcidin Mimetic)	Injectable (Sub-Q)	Iron Overload Disorders				Initiate Phase 1 Clinical Trial in 2017	Worldwide

Our Product Candidates

PTG-100

PTG-100 has first-in-class potential as an oral, α4β7 integrin-specific antagonist peptide for treatment of IBD. The α4β7 integrin is considered to be one of the most GI-specific biological targets for IBD due to its binding to MAdCAM-1, an extracellular protein that resides mostly in the GI vasculature.

We are leveraging several factors to inform and guide the clinical development of PTG-100 for the treatment of IBD. First, PTG-100 shares the same α4β7 integrin target as the injectable antibody drug vedolizumab, marketed as Entyvio®, for the treatment of moderate-to-severe UC and CD. Second, we utilized PD biomarker assays similar to those described in scientific publications with Entyvio® and other antibodies in development as indicators of target engagement to establish POC in our Phase 1 clinical trial with PTG-100. We believe that we can leverage the development and regulatory path of Entyvio® and other approved antibody drugs for IBD.

We have completed extensive pre-clinical studies of PTG-100 in which we established pharmacological POC, including effects on T cell trafficking and mucosal healing similar to a comparator α4β7 rodent antibody, DATK-32. Following the submission and approval of a Clinical Trial Notification (CTN) in Australia in December 2015, we initiated a Phase 1 clinical trial, comprised of single ascending dose (SAD) and multiple ascending dose (MAD) components which evaluated safety, pharmacokinetics (PK), and PD-based POC in healthy subjects using an oral liquid formulation of PTG-100. The trial also included a bridging component which compared the relative bioavailability and PD effects of the liquid formulation and a capsule formulation that we intend to move forward in clinical development. The Phase 1 clinical trial was completed in June 2016. There were no serious adverse events reported in the Phase 1 clinical trial, and no dose-limiting clinical trial toxicities were observed. All reported adverse events were of mild to moderate severity. There were no dose-dependent increases observed for any adverse events. The most frequent adverse events reported by subjects on PTG-100 were headache and upper respiratory tract infection. These events were also observed in subjects who took placebo. The preliminary maximally tolerated dose was established at 1,000 mg, the highest dose tested, for both single and multiple dosing, although no dose-limiting toxicities were observed at the 1,000 mg dose level. In addition, we observed dose-dependent PD effects, including target engagement and pharmacologic activity, similar to what was observed in the pre-clinical setting. Finally, we established that the plasma exposure of the capsule formulation was lower than that of the liquid formulation at the same dose level. The PD effects (target engagement and pharmacologic activity) were highly similar between the two formulations, despite the lower plasma exposure of the capsule formulation. We believe this data will support the introduction of the capsule formulation in the Phase 2b clinical trial. We expect to have final unblinded data from the completed Phase 1 clinical trial by the end of the third quarter of 2016.

We plan to file an IND in the United States by the end of the third quarter of 2016 to support initiation of a global Phase 2b randomized, double-blinded, placebo-controlled dose-finding clinical trial by the end of the fourth quarter of 2016 to assess the safety and efficacy of PTG-100 in approximately 260 moderate-to-severe UC patients. We plan to utilize the same capsule formulation in the Phase 2b trial that was tested in the formulation bridging component of the Phase 1 clinical trial. The primary endpoint of our Phase 2b clinical trial is expected to be the induction of remission, which is consistent with the development of previously approved drugs for UC. We plan to develop PTG-100 initially for the treatment of moderate-to-severe UC, potentially followed by CD and pediatric IBD, the latter being an orphan indication.

PTG-200

Our second oral, GI-restricted peptide product candidate is PTG-200, a potential first-in-class IL-23R specific antagonist for the treatment of IBD. IL-23 is a member of the IL-12 family of pro-inflammatory cytokines, which are proteins that regulate inflammatory and immune function and play a key role in the development of IBD. By blocking the IL-23 receptor with PTG-200 in the GI tissue compartment, we expect to reduce inflammation while potentially minimizing the risk of systemic side effects due to its GI-restricted nature. The IL-23 pathway is targeted by the IL-12 and IL-23 antagonist infused antibody drug ustekinumab marketed as Stelara® for psoriasis and psoriatic arthritis. Stelara® has also recently reported positive Phase 3 clinical trial results in patients with moderate-to-severe CD.

We have completed pre-clinical POC studies for PTG-200, started IND-enabling studies, and plan to initiate a Phase 1 clinical trial in 2017. We plan to develop PTG-200 initially for the treatment of moderate-to-severe CD, potentially followed by UC and pediatric IBD, the latter being an orphan indication.

PTG-300

PTG-300 is an injectable hepcidin mimetic peptide that we are developing for the treatment of iron overload disorders such as transfusion-dependent β-Thalassemia, HH and SCD, each of which may qualify PTG-300 for orphan drug designation. Hepcidin is a peptide hormone critical for regulating iron homeostasis. However, hepcidin has significant stability, potency and solubility limitations. We have discovered and developed PTG-300 as a stable, soluble, hepcidin mimetic that can potentially be more potent and more amenable for weekly or less frequent subcutaneous delivery compared to hepcidin. We plan to complete IND-enabling studies by the end of the first half of 2017 and initiate a Phase 1 clinical trial in 2017.

Our Peptide Technology Platform

Our proprietary peptide technology platform is based on a series of tools and methods which allow us to discover and develop structurally novel oral or injectable peptides as potential product candidates. The platform utilizes these tools and techniques in an integrated and iterative manner in synergy with our deep-rooted knowledge in peptide chemistry, which allows us to arrive at a product with the desired potency, selectivity, oral or plasma stability, PK, and physicochemical properties. These tools and techniques include, but are not limited to, the following:

- *Molecular design tools and large virtual libraries of constrained scaffolds, collectively known as Vectrix*™: Allows for the *de novo* selection of peptide scaffolds as starting points against specific targets.
- *Random libraries and phage display techniques:* Allows for the discovery and optimization of peptide hits.
- *Oral stability assays: In vitro* and *ex vivo* assays and systems that simulate chemical and biological mechanisms, and physical barriers that constrained peptides must overcome for oral stability.
- *Medicinal peptide chemistry:* Allows optimization and refinement of potency, selectivity, oral stability and GI restriction.
- *In vivo pharmacology tools for GI restriction*: Tools to quantify compound concentrations and activity in various GI tissue compartments to develop oral products with minimal systemic exposure.

To date, our platform has generated two oral antagonists peptides, PTG-100 and PTG-200, for IBD, and an injectable hepcidin peptide mimetic, PTG-300, for iron overload disorders, exemplifying our platform's reproducibility and broad scope. We will continue to use our technology platform to discover novel peptides against targets and diseases where oral small molecules or injectable biologics do not offer satisfactory outcomes to patients.

Our Strategy

Our goal is to become a leading biopharmaceutical company by discovering, developing and commercializing first-in-class peptide-based therapeutics that have the potential to transform current treatment paradigms for patients and address unmet medical needs. We are currently pursuing the development of oral peptides that specifically target a number of biological pathways that are also targeted by currently marketed injectable antibody drugs. The critical components of our strategy are as follows:

- **Advance our two lead oral, GI-restricted peptide product candidates, PTG-100 and PTG-200, in clinical development to evaluate the safety, PK, PD-based POC and efficacy in IBD patients.**
  - *PTG-100:* We completed our Phase 1 clinical trial of PTG-100. This clinical trial was designed to evaluate safety and tolerability, PK, and PD-based POC in NHVs, as well as evaluate the relative

bioavailability of our capsule formulation compared to the liquid formulation. We plan to initiate a Phase 2b clinical trial of PTG-100 in patients with moderate-to-severe UC by the end of the fourth quarter of 2016.

- *PTG-200:* We have commenced IND-enabling studies of PTG-200 and plan to initiate a Phase 1 clinical trial in 2017. PTG-200 will initially be developed as a targeted oral therapy for patients with moderate-to-severe CD.

- **Leverage our peptide technology platform to expand our differentiated peptide-based product pipeline across multiple therapeutic areas**.

  - *PTG-300:* We have initiated IND-enabling studies of PTG-300, a subcutaneous (SC), injectable hepcidin mimetic peptide that would be developed for iron overload disorders such as transfusion-dependent β-Thalassemia, HH, and SCD, each of which may qualify PTG-300 for orphan drug designation.

- **Opportunistically expand the value of our oral, GI-restricted peptide product candidates through co-development and regional partnerships.** For PTG-100 and PTG-200, we intend to retain key development and commercialization rights in the United States and build a commercial infrastructure; however, we will consider other strategic opportunities as they arise. We may decide to enter into co-development collaborations in select geographies where we believe a collaborator can bring additional regional development and/or commercial expertise in order to maximize the value of our oral, GI-restricted peptide product candidates.

- **Out-license non-core assets and structure research collaborations based on our proprietary peptide technology platform.** We continually review our internal research priorities and therapeutic focus and may decide to out-license non-core assets that arise from our platform. We may seek research collaborations that leverage the capabilities of our core technology platform in order to monetize and expand upon the breadth of opportunities that may be uniquely accessible through our platform.

- **Protect and leverage our intellectual property portfolio and patents.** We believe that our intellectual property protection strategy, grounded in securing composition of matter patents on the NCEs developed using our technology platform, has best positioned us to gain broad and strong protection of our assets.

- **Leverage the drug discovery, development and commercialization expertise of our management team and network of scientific advisors and key opinion leaders.** We are led by a strong management team with deep experience in drug discovery and development, collaborations, operations and corporate finance. Our team has been involved in a broad spectrum of R&D activities leading to successful outcomes, including FDA approved and marketed drugs. We will continue to leverage the collective experience and talent of our management team, our network of leading scientific experts, and key opinion leaders (KOLs) to strategize and implement our development and commercialization strategy.

Risks Related to Our Business

Our ability to execute our business strategy is subject to numerous risks, as more fully described in the section entitled "Risk Factors" immediately following this prospectus summary. These risks include, among others:

- we have incurred significant losses since our inception. Our net loss for the years ended December 31, 2014 and 2015 was approximately $11.1 million and $14.9 million, respectively, and $11.7 million for the three months ended March 31, 2016. As of March 31, 2016, we had an accumulated deficit of $39.2 million;

- we have never generated any revenue from product sales and may never be profitable;
- we are an early clinical-stage biopharmaceutical company with no approved products and no historical product revenue, which makes it difficult to assess our future prospects and financial results;
- we are heavily dependent on the success of our lead product candidates PTG-100, which is in early-stage clinical development, and PTG-200, which is in pre-clinical development, and the development of other pre-clinical product candidates such as PTG-300;
- we will require substantial additional funding, which may not be available to us on acceptable terms, or at all;
- clinical development is a lengthy and expensive process with an uncertain outcome, and results of earlier studies and trials may not be predictive of future trial results;
- all of our peptide-based product candidates other than PTG-100 are in research or pre-clinical development and have not entered into clinical trials. If we are unable to develop, test, and commercialize our peptide-based product candidates, our business will be adversely affected;
- our proprietary peptide platform is a differentiated approach to the discovery, design, and development of new product candidates and may not result in any products of commercial value;
- the regulatory approval processes of the FDA and comparable foreign authorities are lengthy, time consuming and inherently unpredictable, and if we are ultimately unable to obtain regulatory approval for our product candidates our business will be substantially harmed;
- our product candidates may cause undesirable side effects or have other properties impacting safety that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in limiting the commercial opportunity for our product candidates if approved;
- if we are unable to obtain or protect intellectual property rights related to our product candidates and technologies, we may not be able to compete effectively in our markets;
- we face significant competition from other biotechnology and pharmaceutical companies, and our operating results will suffer if we fail to compete effectively; and
- we rely completely on third parties to manufacture our drug substance and clinical drug product and we intend to rely on third parties to produce commercial supplies of any approved peptide-based product candidate.

Corporate Information

Protagonist Pty Limited (Protagonist Australia) was incorporated in Australia in September 2001. We were incorporated under the laws of the State of Delaware in 2006, under the name Protagonist Therapeutics, Inc., and became the parent of Protagonist Australia pursuant to a transaction in which all of the issued and outstanding capital stock of Protagonist Australia was exchanged for shares of our common stock and Series A preferred stock. Our principal executive offices are located at 521 Cottonwood Drive, Suite 100, Milpitas, California 95035. Our telephone number is (408) 649-7370. Our website address is www.protagonist-inc.com. The information contained in, or accessible through, our website does not constitute part of this prospectus, should not be relied on in determining whether to make an investment decision, and the inclusion of our website address in this prospectus is an inactive textual reference only.

Implications of Being an Emerging Growth Company

We are an "emerging growth company" as defined in the Jumpstart Our Business Startups Act (JOBS Act), enacted in April 2012. An emerging growth company may take advantage of reduced reporting requirements that are otherwise applicable to public companies. These provisions include, but are not limited to:

- being permitted to present only two years of audited financial statements and only two years of related Management's Discussion & Analysis of Financial Condition and Results of Operations in this prospectus;
- not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002, as amended (Sarbanes-Oxley Act);
- reduced disclosure obligations regarding executive compensation in our periodic reports, proxy statements and registration statements; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

We may take advantage of these provisions until we cease to be an "emerging growth company." We will cease to be an "emerging growth company" upon the earliest of: (1) the last day of the fiscal year following the fifth anniversary of this offering, (2) the last day of the first fiscal year in which our annual gross revenues are $1.0 billion or more, (3) the date on which we have, during the previous rolling three-year period, issued more than $1.0 billion in non-convertible debt securities, and (4) the date on which we are deemed to be a "large accelerated filer" as defined in the Securities Exchange Act of 1934, as amended (Exchange Act).

We have elected to take advantage of certain of the reduced disclosure obligations available to emerging growth companies the registration statement of which this prospectus is a part and may elect to take advantage of other reduced reporting requirements in future filings. As a result, the information that we provide to our stockholders may be different than you might receive from other public reporting companies in which you hold equity interests.

In addition, the JOBS Act provides that an "emerging growth company" can take advantage of an extended transition period for complying with new or revised accounting standards. This provision allows an emerging growth company to delay the adoption of some accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of delayed adoption of new or revised accounting standards and, therefore, we will be subject to the same requirements to adopt new or revised accounting standards as other public companies that are not "emerging growth companies."

The Offering

Common stock offered by us	5,835,000 shares.
Common stock to be outstanding after this offering	14,658,551 shares (15,533,801 shares if the underwriters exercise their option to purchase additional shares in full).
Underwriters' option to purchase additional shares	The underwriters have an option for a period of 30 days to purchase up to 875,250 additional shares of our common stock.
Use of proceeds	We estimate that the net proceeds from this offering, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us, will be approximately $62.0 million, or approximately $71.8 million if the underwriters exercise their option to purchase additional shares from us in full, assuming an initial public offering price of $12.00 per share, the midpoint of the price range set forth on the cover page of this prospectus. We intend to use the net proceeds from this offering to fund continued development of PTG-100 through the completion of a Phase 2b clinical trial, to advance PTG-200 to complete IND-enabling studies and to begin a Phase 1 clinical trial, to advance PTG-300 to complete IND-enabling studies, to fund our research and discovery activities related to additional product candidates and for working capital and other general corporate purposes. See "Use of Proceeds" for a more complete description of the intended use of proceeds from this offering.
Risk Factors	You should read the "Risk Factors" section of this prospectus and the other information in this prospectus for a discussion of factors to consider carefully before deciding to invest in shares of our common stock.
Proposed NASDAQ Global Market Symbol	"PTGX"

The number of shares of common stock to be outstanding after this offering is based on 8,823,551 shares of our common stock (including redeemable convertible preferred stock on an as-converted basis) outstanding at March 31, 2016, and excludes the following:

- 783,341 shares of our common stock issuable upon exercise of stock options outstanding under our 2007 Stock Option and Incentive Plan (2007 Plan), as amended, at a weighted average exercise price of $1.32 per share;
- 582,582 shares of our common stock issuable upon the exercise of stock options granted after March 31, 2016 at a weighted-average exercise price of $4.39 per share;
- 1,999,998 shares of redeemable preferred stock (convertible into 137,930 shares of common stock) issued pursuant to the exercise of preferred stock warrants after March 31, 2016;
- 52,948 shares of common stock reserved for issuance pursuant to future awards under our 2007 Plan, which will become available for issuance under our 2016 Equity Incentive Plan upon completion of this offering;

- 1,200,000 shares of common stock reserved, subject to increase on an annual basis, reserved for future issuance pursuant to our 2016 Equity Incentive Plan, which will become effective upon the consummation of this offering as well as any automatic increases in the number of shares of common stock reserved for future issuance under this benefit plan; and
- 150,000 shares of our common stock reserved for future issuance under our 2016 Employee Stock Purchase Plan (2016 ESPP), which will become effective upon the consummation of this offering, as well as any automatic increases in the number of shares of common stock reserved for future issuance under this benefit plan.

Unless otherwise indicated, all information in this prospectus assumes:

- a 14.5-for-1 reverse split of our outstanding common stock prior to completion of this offering;
- the filing of our amended and restated certificate of incorporation and the adoption of our amended and restated bylaws, which will occur immediately prior to the consummation of this offering;
- the conversion of all outstanding shares of our redeemable convertible preferred stock as of March 31, 2016 into 8,439,641 shares of our common stock upon the completion of this offering;
- no exercise of the outstanding options and warrants subsequent to March 31, 2016; and
- no exercise by the underwriters of their option to purchase additional shares of our common stock.

Certain of our existing stockholders and their affiliated entities, including investors affiliated with certain of our directors, have indicated an interest in purchasing an aggregate of up to approximately $40.0 million in shares of our common stock in this offering at the initial public offering price and on the same terms as the other purchasers in this offering. However, because indications of interest are not binding agreements or commitments to purchase, these investors may determine to purchase fewer shares than they indicate an interest in purchasing or not to purchase any shares in this offering. It is also possible that these investors could indicate an interest in purchasing more shares of our common stock. In addition, the underwriters could determine to sell fewer shares to any of these investors than the investors indicate an interest in purchasing or not to sell any shares to these investors.

On August 1, 2016, we effected a 14.5-for-1 reverse split of our common stock. Upon the effectiveness of the reverse stock split, (i) every 14.5 shares of outstanding common stock was combined into 1 share of common stock, (ii) the number of shares of common stock for which each outstanding option to purchase common stock is exercisable was proportionally decreased on a 14.5-for-1 basis, (iii) the exercise price of each outstanding option to purchase common stock was proportionately increased on a 14.5-for-1 basis, and (iv) the conversion ratio for each share of outstanding preferred stock which is convertible into the Company's common stock was proportionately reduced on a 14.5-for-1 basis. All of the outstanding common stock share numbers (including shares of common stock into which the Company's outstanding preferred stock shares are convertible), share prices, exercise prices and per share amounts have been adjusted in this prospectus, on a retroactive basis, to reflect this 14.5-for-1 reverse stock split for all periods presented. The par value per share and the authorized number of shares of common stock and preferred stock were not adjusted as a result of the reverse stock split.

SUMMARY CONSOLIDATED FINANCIAL DATA

The following tables summarize our consolidated financial data. We have derived the consolidated statements of operations data for the years ended December 31, 2014 and 2015, from our audited consolidated financial statements included elsewhere in this prospectus. We have derived the summary consolidated statements of operations data for the three months ended March 31, 2015 and 2016, and the summary consolidated balance sheet data as of March 31, 2016, from our unaudited interim condensed consolidated financial statements included elsewhere in this prospectus. We have prepared the unaudited interim condensed consolidated financial statements on the same basis as the audited consolidated financial statements and have included, in our opinion, all adjustments, consisting only of normal recurring adjustments that we consider necessary for a fair statement of the financial information set forth in those statements. Our historical results are not necessarily indicative of the results that may be expected in the future and our interim results for the three months ended March 31, 2016 are not necessarily indicative of results to be expected for the full year ending December 31, 2016, or any other period. You should read this data together with our consolidated financial statements and related notes, "Selected Consolidated Financial Data," and "Management's Discussion and Analysis of Financial Condition and Results of Operations" included elsewhere in this prospectus.

	Year Ended December 31,		Three Months Ended March 31,	
	2014	2015	2015	2016
	(In thousands, except share and per share data)			
Consolidated Statements of Operations Data:				
Operating expenses:				
Research and development	$ 7,459	$ 11,831	$ 2,183	$ 5,625
General and administrative	1,860	2,963	506	1,415
Total operating expenses	9,319	14,794	2,689	7,040
Loss from operations	(9,319)	(14,794)	(2,689)	(7,040)
Interest income	16	19	1	12
Change in fair value of redeemable convertible preferred stock tranche and warrant liabilities	(1,769)	(83)	(9)	(4,719)
Net loss	$ (11,072)	$ (14,858)	$ (2,697)	$ (11,747)
Net loss attributable to common stockholders[(1)]	$ (11,218)	$ (14,933)	$ (2,697)	$ (11,787)
Net loss per share attributable to common stockholders, basic and diluted[(1)]	$ (49.38)	$ (59.32)	$ (11.75)	$ (40.96)
Weighted-average shares used to compute net loss per share attributable to common stockholders, basic and diluted[(1)]	227,197	251,717	229,483	287,800
Pro forma net loss per share, basic and diluted (unaudited)[(1)]		$ (3.57)		$ (1.91)
Pro forma weighted-average shares used to compute net loss per share, basic and diluted (unaudited)[(1)]		4,313,032		5,884,892

(1) See Notes 2, 13, and 14 to our audited consolidated financial statements and Note 12 to our unaudited interim condensed consolidated financial statements included elsewhere in this prospectus for an explanation of the calculations of our basic and diluted net loss per share attributable to common stockholders, pro forma net loss per common share, and the weighted-average number of shares used in the computation of the per share amounts.

	As of March 31, 2016		
	Actual	Pro Forma(1)	Pro Forma As Adjusted(2)(3)
		(Unaudited) (In thousands)	
Consolidated Balance Sheet Data:			
Cash, cash equivalents and available-for-sale securities	$ 29,022	$ 29,022	$ 91,041
Working capital	26,467	26,467	88,486
Total assets	31,856	31,856	93,875
Redeemable convertible preferred stock warrant liability	1,005	—	—
Redeemable convertible preferred stock	65,361	—	—
Accumulated deficit	(39,162)	(39,162)	(39,162)
Total stockholders' (deficit) equity	(38,980)	27,386	89,405

(1) The pro forma column reflects (i) the conversion of all outstanding shares of our redeemable convertible preferred stock as of March 31, 2016 into 8,439,641 shares of our common stock immediately prior to the closing of this offering, and (ii) the reclassification of the redeemable convertible preferred stock warrant liability to consolidated stockholders' equity upon the completion of this offering, as the warrants to purchase redeemable convertible preferred stock will be exercised, converted into warrants to purchase common stock or expired unexercised on May 10, 2016.

(2) The pro forma as adjusted column reflects the pro forma adjustments set forth above and the receipt of $62.0 million in net proceeds from our sale of shares of common stock in this offering at an assumed initial public offering price of $12.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us.

(3) Each $1.00 increase (decrease) in the assumed initial public offering price of $12.00 per share would increase (decrease), the amount of cash, cash equivalents and available-for-sale securities, working capital, total assets and total stockholders' equity by $5.4 million, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us. We may also increase or decrease the number of shares we are offering. An increase (decrease) of 1,000,000 shares in the assumed number of shares we are offering would increase (decrease) the amount of cash, cash equivalents and available-for-sale securities, working capital, total assets and stockholders' equity by approximately $11.2 million, assuming the assumed initial public offering price per share, as set forth on the cover page of this prospectus, remains the same. The pro forma as adjusted information is illustrative only, and we will adjust this information based on the actual initial public offering price and other terms of this offering determined at pricing.

RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below, together with the other information contained in this prospectus, including "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our consolidated financial statements and the related notes appearing at the end of this prospectus, before making your decision to invest in our common stock. We cannot assure you that any of the events discussed in the risk factors below will not occur. The occurrence of any of the events or developments described below could have a material and adverse impact on our business, results of operations, financial condition, and cash flows and future prospects and, if so, our future prospects would likely be materially and adversely affected. If any of such events were to happen, the trading price of our common stock could decline, and you could lose all or part of your investment. Although we have discussed all known material risks, the risks described below are not the only ones that we may face, and additional risks or uncertainties not known to us or that we currently deem immaterial may also impair our business and future prospects.

Risks Related to Our Financial Position and Capital Requirements

We have incurred significant losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future. We have never generated any revenue from product sales and may never be profitable.

We have incurred significant operating losses since our inception in 2006. Our net loss for the years ended December 31, 2014 and 2015 was approximately $11.1 million and $14.9 million, respectively, and $11.7 million for the three months ended March 31, 2016. As of March 31, 2016, we had an accumulated deficit of $39.2 million. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' deficit and working capital. We expect to continue incurring significant research, development and other expenses related to our ongoing operations and product development, and as a result, we expect to continue incurring losses for the foreseeable future. We also expect these losses to increase as we continue our development of, and seek regulatory approvals for, our peptide-based product candidates.

We do not anticipate generating revenue from sales of products for the foreseeable future, if ever, and we do not currently have any product candidates in registration or pivotal clinical trials. If any of our peptide-based product candidates fail in clinical trials or do not gain regulatory approval, or even if approved, fail to achieve market acceptance, we may never become profitable. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Failure to become and remain profitable may adversely affect the market price of our common stock and our ability to raise capital and continue operations.

If one or more of our peptide-based product candidates is approved for commercial sale and we retain commercial rights, we anticipate incurring significant costs associated with manufacturing and commercializing such approved peptide-based product candidate. Therefore, even if we are able to generate revenue from the sale of any approved product, we may never become profitable.

We are an early clinical-stage biopharmaceutical company with no approved products and no historical product revenue, which makes it difficult to assess our future prospects and financial results.

We are an early clinical-stage biopharmaceutical company with a limited operating history upon which you can evaluate our business and prospects. Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of uncertainty. Our operations to date have been limited to developing our technology, undertaking pre-clinical studies and clinical trials of our pipeline candidates, including pre-clinical studies and clinical trial of PTG-100 and pre-clinical studies of PTG-200 and PTG-300, as well as our proprietary technology platform. We have successfully filed a CTN in Australia to support the Phase 1 clinical trial of PTG-100. To date, we have not filed a U.S. Investigational New Drug (IND) application

for any of our product candidates and have only commenced human clinical trials in PTG-100. As an early clinical-stage company, we have not yet demonstrated an ability to generate revenue or successfully overcome many of the risks and uncertainties frequently encountered by companies in new and rapidly evolving fields such as biopharmaceutical drug discovery and development. Consequently, the ability to accurately assess our future operating results or business prospects is significantly more limited than if we had a longer operating history or approved products on the market.

We expect that our financial condition and operating results will fluctuate significantly from period to period due to a variety of factors, many of which are beyond our control, including, but not limited to:

- the clinical outcomes from the continued development of our product candidates;
- potential side effects of our product candidates that could delay or prevent approval or cause an approved drug to be taken off the market;
- our ability to obtain, as well as the timeliness of obtaining, additional funding to develop, and potentially manufacture and commercialize our product candidates;
- competition from existing products directed against the same biological target or therapeutic indications of our product candidates as well as new products that may receive marketing approval;
- the entry of generic versions of products that compete with our product candidates;
- the timing of regulatory review and approval of our product candidates;
- market acceptance of our product candidates that receive regulatory approval, if any;
- our ability to establish an effective sales and marketing infrastructure directly or through collaborations with third parties;
- the ability of patients or healthcare providers to obtain coverage or sufficient reimbursement for our products;
- whether Johnson & Johnson Development Corporation (JJDC) decides to exercise its rights of first negotiation on any of our assets that are subject to the Letter Agreement with JJDC, including PTG-200, and we have to negotiate with JJDC for prolonged periods pursuant to the aforementioned agreement;
- the ability of third party manufacturers to manufacture in accordance with current good manufacturing practices (GMP) our product candidates for the conduct of clinical trials and, if approved, for successful commercialization;
- our ability as well as the ability of any third party collaborators, to obtain, maintain and protect intellectual property rights covering our product candidates and technologies, and our ability to develop, manufacture and commercialize our product candidates without infringing on the intellectual property rights of others;
- our ability to add infrastructure and manage adequately our future growth; and
- our ability to attract and retain key personnel with appropriate expertise and experience to manage our business effectively.

Accordingly, the likelihood of our success must be evaluated in light of many potential challenges and variables associated with an early-stage biopharmaceutical company, many of which are outside of our control, and past results, including operating or financial results, should not be relied on as an indication of future results.

We will require substantial additional funding, which may not be available to us on acceptable terms, or at all.

Our operations have consumed substantial amounts of cash since inception. We conducted a Phase 1 clinical trial of PTG-100 in healthy volunteers and we are preparing to conduct a Phase 2b clinical trial of PTG-100 in patients with moderate-to-severe ulcerative colitis (UC), and we have also commenced IND-enabling studies of PTG-200 and PTG-300. Developing pharmaceutical product candidates, including conducting pre-clinical studies and clinical trials, is expensive. We will require substantial additional future capital in order to complete clinical development and, if we are successful, to commercialize any of our current product candidates. If the U.S. Food and Drug Administration (FDA) or any foreign regulatory agency, such as the European Medicines Agency (EMA), requires that we perform studies or trials in addition to those that we currently anticipate with respect to the development of PTG-100, PTG-200 or any of our other product candidates, or repeat studies or trials, our expenses would further increase beyond what we currently expect, and any delay resulting from such further or repeat studies or trials could also result in the need for additional financing.

Upon the completion of this offering, based upon our current operating plan and expected expenditures, we believe that the net proceeds from this offering and our existing cash, cash equivalents, and available-for-sale securities will be sufficient to fund our operations for at least the next 18 months. This period could be shortened if there are any significant increases beyond our expectations in spending on development programs or more rapid progress of development programs than anticipated. Our existing capital resources, including the net proceeds from this offering, will not be sufficient to enable us to initiate any pivotal clinical trials. Accordingly, we expect that we will need to raise substantial additional funds in the future in order to complete clinical development or commercialize any of our product candidates. Our funding requirements and the timing of our need for additional capital are subject to change based on a number of factors, including:

- the rate of progress and the cost of our studies of PTG-100, PTG-200, and PTG-300 and any other product candidates;
- the number of product candidates that we intend to develop using our technology platform;
- the costs of research and pre-clinical studies to support the advancement of other product candidates into clinical development;
- the timing of, and costs involved in, seeking and obtaining approvals from the FDA and comparable foreign regulatory authorities, including the potential by the FDA or comparable regulatory authorities to require that we perform more studies than those that we current expect;
- the costs of preparing to manufacture PTG-100 or PTG-200 on a scale sufficient to enable large-scale clinical trials and commercial supply;
- the timing and cost of transitioning our product formulations into the formulations we intend to use in registration trials and commercialize;
- the costs of commercialization activities if PTG-100 or PTG-200 or any future product candidate is approved, including the formation of a sales force;
- the degree and rate of market acceptance of any products launched by us or our partners;
- the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights;
- our need and ability to hire and retain additional personnel;
- our ability to enter into additional collaboration, licensing, commercialization or other arrangements and the terms and timing of such arrangements; and
- the emergence of competing technologies or other adverse market developments.

If we are unable to obtain additional funding from equity offerings or debt financings, including on a timely basis, we may be required to:

- seek collaborators for one or more of our peptide-based product candidates at an earlier stage than otherwise would be desirable or on terms that are less favorable than might otherwise be available;
- relinquish or license on unfavorable terms our rights to technologies or peptide-based product candidates that we otherwise would seek to develop or commercialize ourselves; or
- significantly curtail one or more of our research or development programs or cease operations altogether.

Raising additional capital may cause dilution to our existing stockholders, restrict our operations or require us to relinquish rights to our peptide-based product candidates or technologies.

We may seek additional funding through a combination of equity offerings, debt financings, collaborations and/or licensing arrangements. Additional funding may not be available to us on acceptable terms, or at all. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted, and the terms may include liquidation or other preferences that adversely affect your rights as a stockholder. The incurrence of indebtedness and/or the issuance of certain equity securities could result in fixed payment obligations and could also result in certain additional restrictive covenants, such as limitations on our ability to incur debt and/or issue additional equity, limitations on our ability to acquire or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. In addition, the issuance of additional equity securities by us, or the possibility of such issuance, may cause the market price of our common stock to decline. In the event that we enter into collaborations and/or licensing arrangements in order to raise capital, we may be required to accept unfavorable terms, including relinquishing or licensing to a third party on unfavorable terms our rights to our proprietary technology platform or peptide-based product candidates that we otherwise would seek to develop or commercialize ourselves or potentially reserve for future potential arrangements when we might be able to achieve more favorable terms.

Risks Related to Our Business and Industry

We are heavily dependent on the success of our lead product candidates, PTG-100, which is in early-stage clinical development, and PTG-200, which is in pre-clinical development, and the development of other product candidates such as PTG-300, and if any of these products fail to receive regulatory approval or are not successfully commercialized, our business would be adversely affected.

We currently have no product candidates that are in registration or pivotal clinical trials or are approved for commercial sale, and we may never be able to develop a marketable product. We expect that a substantial portion of our efforts and expenditures over the next few years will be devoted to our lead product candidates, PTG-100 and PTG-200 targeting inflammatory bowel disease (IBD), and the development of other product candidates such as PTG-300 which targets iron overload disorders. We cannot be certain that PTG-100, PTG-200, PTG-300 or any other product candidates will receive regulatory approval or, if approved, be successfully commercialized. The research, testing, manufacturing, labeling, approval, sale, marketing and distribution of PTG-100, PTG-200, and PTG-300 will remain subject to extensive regulation by the FDA and other regulatory authorities in the United States and other countries, each of which has differing regulations. In addition, even if approved, our pricing and reimbursement will be subject to further review and discussions with payors. We are not permitted to market any product candidate in the United States until after approval of a new drug application (NDA) from the FDA, or in any foreign countries until after approval of a marketing application by corresponding regulatory authorities. We completed a Phase 1 clinical trial for PTG-100 in June 2016. We will need to conduct larger, more extensive clinical trials in the target patient population to support a potential application for regulatory approval by the FDA or corresponding regulatory authorities, and we do not expect to be in a position to do so for the near term. We will not receive any preferential or expedited review of any application for regulatory approval by virtue of the fact that our product candidates target biological pathways that are also targeted by currently marketed injectable antibody drugs, and our product candidates will be subject to the regulatory review processes applicable to completely new drugs.

We have not previously submitted an NDA to the FDA, or similar drug approval filings to comparable foreign authorities, for any product candidate, and we cannot be certain that any of our product candidates will be successful in clinical trial or receive regulatory approval. Filing an application and obtaining regulatory approval for a pharmaceutical product candidate is an extensive, lengthy, expensive and inherently uncertain process, and the regulatory authorities may delay, limit or deny approval of our product candidates for many reasons, including:

- we may not be able to demonstrate that any of our product candidates is safe and effective to the satisfaction of the FDA or comparable foreign regulatory authorities;
- the FDA or comparable foreign regulatory authorities may require additional pre-clinical studies or clinical trials prior to granting approval, which would increase our costs and extend the pre-approval development process;
- the results of our clinical trials may not meet the level of statistical or clinical significance required by the FDA or comparable foreign regulatory authorities for approval;
- the FDA may disagree with the number, design, size, conduct or statistical analysis of one or more of our clinical trials;
- contract research organizations (CROs) that we retain to conduct clinical trials may take actions outside of our control that materially and adversely impact our clinical trials;
- the FDA or comparable foreign regulatory authorities may disagree with, or not accept, our interpretation of data from our pre-clinical studies and clinical trials;
- the FDA may require development of a costly and extensive risk evaluation and mitigation strategy (REMS), as a condition of approval;
- the FDA may identify deficiencies in our manufacturing processes or facilities or those of our third-party manufacturers which would be required to be corrected prior to regulatory approval;
- the success or further approval of competitor products approved in indications in which we undertake development of our product candidates may change the standard of care or change the standard for approval of our product candidate in our proposed indications;
- the FDA or comparable foreign regulatory authorities may change their approval policies or adopt new regulations; and
- relative bioavailability data in monkeys or humans from the formulation bridging component of our Phase 1 trial may not support introduction of the capsule formulation into the Phase 2b clinical trial of PTG-100 or the FDA may find the data inadequate and request another trial.

Our peptide-based product candidates will require additional research, clinical development, manufacturing activities, regulatory approval in multiple jurisdictions (if regulatory approval can be obtained at all), securing sources of commercial manufacturing supply and building of or partnering with a commercial organization. We cannot assure you that our clinical trials for PTG-100 or our planned clinical trials for PTG-200 will be initiated or completed in a timely manner or successfully, or at all. Further we cannot be certain that we plan to advance any other peptide-based product candidates into clinical trials. Moreover, any delay or setback in the development of any product candidate, in particular PTG-100, PTG-200, or PTG-300, would be expected to adversely affect our business and cause our stock price to fall.

The regulatory approval processes of the FDA and comparable foreign authorities are lengthy, time consuming and inherently unpredictable, and if we are ultimately unable to obtain regulatory approval for our product candidates, our business will be substantially harmed.

Our business and future profitability is substantially dependent on our ability to successfully develop, obtain regulatory approval for and then successfully commercialize our most advanced peptide-based product candidates, PTG-100, which has completed a Phase 1 clinical trial for UC, and PTG-200 and PTG-300, which are in pre-clinical development. We have not yet filed an IND for any of our product candidates. We are not permitted to market or promote any of our peptide-based product candidates before we receive regulatory approval from the FDA, the EMA or any other foreign regulatory authority, and we may never receive such regulatory approval for any of our peptide-based product candidates. The time required to obtain approval by the FDA and comparable foreign authorities is unpredictable, typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of regulatory authorities. Approval policies, regulations and the types and amount of clinical and manufacturing data necessary to gain approval may change during the course of clinical development and may vary among jurisdictions. We have not obtained regulatory approval for any product candidate and it is possible that none of our existing product candidates or any product candidates we have in development or may seek to develop in the future will ever obtain regulatory approval.

Our product candidates could fail to receive regulatory approval for many reasons, including the following:

- the FDA or comparable foreign regulatory authorities may disagree with the design or implementation of our clinical trials;
- we may be unable to demonstrate to the satisfaction of the FDA or comparable foreign regulatory authorities that a product candidate is safe and effective for its proposed indication;
- the results of clinical trials may fail to achieve the level of statistical significance required by the FDA or comparable foreign regulatory authorities for approval;
- we may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- the FDA or comparable foreign regulatory authorities may disagree with our interpretation of data submitted in support of regulatory approval;
- the data collected from pre-clinical studies and clinical trials of our peptide-based product candidates may not be sufficient to support the submission of an NDA, supplemental NDA, Biologics License Application (BLA) or other regulatory submissions necessary to obtain regulatory approval in the United States or elsewhere;
- we or our contractors may not meet the GMP and other applicable requirements for manufacturing processes, procedures, documentation and facilities necessary for approval by the FDA or comparable foreign regulatory authorities; and
- changes to the approval policies or regulations of the FDA or comparable foreign regulatory authorities with respect to our product candidates may result in our clinical data becoming insufficient for approval.

The lengthy regulatory approval process as well as the unpredictability of future clinical trial results may result in our failing to obtain regulatory approval to market PTG-100 and PTG-200, our lead product candidates, or any other product candidate, such as PTG-300, which would harm our business, results of operations and prospects significantly.

In addition, even if we were to obtain regulatory approval, regulatory authorities may approve our product candidates for fewer or more limited indications than what we requested approval for, may include safety warnings or other restrictions that may negatively impact the commercial viability of or product candidates, including the potential for a favorable price or reimbursement at a level that we would otherwise intend to charge

for our products. Likewise, regulatory authorities may grant approval contingent on the performance of costly post-marketing clinical trials or the conduct of an expensive REMS, which could significantly reduce the potential for commercial success or viability of our product candidates. Any of the foregoing possibilities could materially harm the prospects for our product candidates and business and operations.

We have not previously submitted an NDA, a BLA, a Marketing Authorization Application (MAA), or any corresponding drug approval filing to the FDA, the EMA or any comparable foreign authority for any peptide-based product candidate. Further, our product candidates may not receive regulatory approval even we complete such filing. If we do not receive regulatory approvals for our product candidates, we may not be able to continue our operations.

Clinical development is a lengthy and expensive process with an uncertain outcome, and results of earlier studies and trials may not be predictive of future trial results. Clinical failure can occur at any stage of clinical development. Further, we have never conducted a Phase 2 or Phase 3 clinical trial or submitted a NDA.

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical development process. The results of pre-clinical studies and early clinical trials of our product candidates and studies and trials of other products may not be predictive of the results of later-stage clinical trials. In addition to our planned pre-clinical studies and clinical trials, we expect to have to complete at least two large scale, or adequate, well-controlled trials to demonstrate substantial evidence of efficacy and safety for each product candidate we intend to commercialize. Further, given the patient populations for which we are developing therapeutics, we expect to have to evaluate long-term exposure to establish the safety of our therapeutics in a chronic dose setting. We have never conducted a Phase 2 or Phase 3 clinical trial or submitted a NDA, and as a result, we have no history or track-record to rely on when entering these phases of the development cycle. For example, the results generated to date in pre-clinical studies and the Phase 1 clinical trial for PTG-100 do not ensure that future Phase 2 clinical trials or later clinical trials will have similar results or be successful. Product candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through pre-clinical studies and initial clinical trials. Clinical trial failures may result from a multitude of factors including, but not limited to, flaws in trial design, dose selection, placebo effect, patient enrollment criteria and failure to demonstrate favorable safety and/or efficacy traits of the product candidate. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier trials. Based upon negative or inconclusive results, we may decide, or regulators may require us, to conduct additional clinical trials or pre-clinical studies.

We may experience delays in ongoing clinical trials, and we do not know whether planned clinical trials will begin on time, need to be redesigned, enroll patients on time or be completed on schedule, if at all. Clinical trials can be delayed for a variety of reasons, including delays related to:

- obtaining regulatory approvals to commence a clinical trial;
- reaching agreement on acceptable terms with prospective CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- fraud or negligence on the part of CRO, contract manufacturing organizations (CMOs), consultants or contractors;
- obtaining institutional review board (IRB) or ethics committee (EC), approval at each site;
- recruiting suitable patients to participate in a clinical trial;
- having patients complete a clinical trial or return for post-treatment follow-up;
- clinical sites deviating from the clinical trial's protocol or dropping out of a clinical trial;

- adding new clinical trial sites; or
- manufacturing sufficient quantities of product candidate for use in clinical trials.

We could encounter delays if a clinical trial is modified, suspended or terminated by us, by the IRBs or ECs of the institutions in which such clinical trials are being conducted, by a Data Safety Monitoring Board, for such trial or by the FDA or other regulatory authorities. Such authorities may impose a modification, suspension or termination due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical trial protocols, inspection of the clinical trial operations or clinical trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a drug, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. If we experience delays in the completion of, or termination of, any clinical trial of our product candidates, the commercial prospects of our product candidates will be harmed and our ability to generate product revenue from any of these product candidates will be delayed. In addition, any delays in completing our clinical trials will increase our costs, slow down our product candidate development and approval process and jeopardize our ability to commence product sales and generate revenue. Any of these occurrences may harm our business, financial condition and prospects significantly. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our product candidates.

In addition, data obtained from trials and studies are susceptible to varying interpretations, and regulators may not interpret our data as favorably as we do, which may delay, limit or prevent regulatory approval.

Enrollment and retention of patients in clinical trials is an expensive and time-consuming process and could be made more difficult or rendered impossible by multiple factors outside our control.

We may encounter delays in enrolling, be unable to enroll or maintain, a sufficient number of patients to complete any of our clinical trials. Patient enrollment and retention in clinical trials is a significant factor in the timing of clinical trials and depends on many factors, including the size and nature of the patient population, the nature of the trial protocol, the existing body of safety and efficacy data with respect to the study drug, the number and nature of competing treatments and ongoing clinical trials of competing drugs for the same indication, the proximity of patients to clinical trial sites and the eligibility criteria for the clinical trial. Furthermore, any negative results we may report in clinical trials of our product candidates may make it difficult or impossible to recruit and retain patients in other clinical trials of that same candidate. For example, we are aware of a number of therapies that are commercialized or are being developed for IBD and we expect to face competition from these investigational drugs or approved drugs for potential subjects in our clinical trials, which may delay the pace of enrollment in our planned clinical trials. Delays or failures in planned patient enrollment or retention may result in increased costs, program delays or both, which could have a harmful effect on our ability to develop our product candidates, or could render further development impossible.

All of our peptide-based product candidates other than PTG-100 are in research or pre-clinical development and have not entered into clinical trials. If we are unable to develop, test and commercialize our peptide-based product candidates, our business will be adversely affected.

As part of our strategy, we also seek to discover, develop and commercialize a portfolio of new peptide-based product candidates in addition to PTG-100. Research programs to identify appropriate biological targets pathways and product candidates require substantial scientific, technical, financial and human resources, whether or not any product candidates are ultimately identified. Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for many reasons, including:

- our financial and internal resources are insufficient;

- our research methodology used may not be successful in identifying potential product candidates;
- competitors may develop alternatives that render our product candidates uncompetitive;
- our other product candidates may be shown to have harmful side effects or other characteristics that indicate such product candidate is unlikely to be effective or otherwise unlikely to achieve applicable regulatory approval;
- our product candidates may not be capable of being produced in commercial quantities at an acceptable cost, or at all; or
- a product candidate may not be accepted by patients, the medical community, healthcare providers or third-party payors.

Our research and development strategy for our lead product candidates relies in large part on clinical data and results obtained from antibody and small molecule products that are approved or in late-stage development that could ultimately prove to be inaccurate or unreliable for use with our peptide-based product candidate approach.

As part of our strategy to mitigate clinical development risk, we seek to develop peptide-based product candidates against biological targets and pathways which have been identified as addressable by approved or later stage products in development. While we utilize pre-clinical *in vivo* and *in vitro* models as well as clinical biomarkers to assess potential safety and efficacy early in the candidate selection and development process, this strategy necessarily relies upon clinical data and other results obtained by third parties that may ultimately prove to be inaccurate or unreliable or otherwise not applicable to the indications in which we develop our peptide-based product candidates. We will have to conduct clinical trials to show the safety and efficacy of our peptide-based product candidates against the identified biological targets and pathways to show that our peptide-based product candidates can address the identified mechanism of action shown by these third party results. For example, PTG-100 is an $\alpha 4\beta 7$ integrin antagonist that targets the same target as the currently marketed injectable antibody drug, Entyvio®, and PTG-200 targets the IL-23 biological pathway, which is a pathway targeted by the currently marketed injectable antibody drug, Stelara®, approved in a different indication and which has demonstrated positive results in a Phase 3 clinical trial in IBD. If our interpretation of the third party clinical data and results from molecules directed against the same biological target or pathway or our pre-clinical *in vivo* and *in vitro* models prove inaccurate or our assumptions and conclusions about the applicability of our peptide-based product candidates against the same biological targets or pathways are incorrect or inaccurate, then our development efforts may prove longer and more extensive and our research and development strategy and business and operations could be significantly harmed.

Our proprietary peptide platform may not result in any products of commercial value.

We have developed a proprietary peptide technology platform to enable the identification, testing, design and development of new product candidates. We cannot assure you that our peptide platform will work, nor that any of these potential targets or other aspects of our proprietary drug discovery and design platform will yield product candidates that could enter clinical development and, ultimately, be commercially valuable. Although we expect to continue to enhance the capabilities of our proprietary platform by developing and integrating existing and new research technologies, we may not be successful in any of our enhancement and development efforts. For example, we may not be able to enter into agreements on suitable terms to obtain technologies required to develop certain capabilities of our peptide platform. In addition, we may not be successful in developing the conditions necessary to simulate specific tissue function from multiple species, or otherwise develop assays or cell cultures necessary to expand these capabilities. If our enhancement or development efforts are unsuccessful, we may not be able to advance our drug discovery capabilities as quickly as we expect or identify as many potential drug candidates as we desire.

Our product candidates may cause undesirable side effects or have other properties impacting safety that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in limiting the commercial opportunity for our product candidates if approved.

Undesirable side effects that may be caused by our product candidates or caused by similar approved drugs or product candidates in development by other companies, could cause us or regulatory authorities to interrupt, delay or halt clinical trials and could result in a more restrictive label or the delay or denial of regulatory approval by the FDA or other comparable foreign authorities. Results of our clinical trials could reveal a high and unacceptable severity and prevalence of side effects or adverse events related to our product candidates. In such an event, our clinical trials could be suspended or terminated and the FDA or comparable foreign regulatory authorities could order us to cease further development of our product candidates for any or all targeted indications. In addition, drug-related side effects could negatively affect patient recruitment or the ability of enrolled patients to complete the trial and even if our clinical trials are completed and our product candidate is approved, drug-related side effects could restrict the label or result in potential product liability claims. Any of these occurrences could significantly harm our business, financial condition and prospects significantly.

Moreover, since our product candidates PTG-100 and PTG-200 are being developed for indications for which injectable antibody drugs have been approved, we expect that our clinical trials would need to show a risk/benefit profile that is competitive with those existing products and product candidates in order to obtain regulatory approval or, if approved, a product label that is favorable for commercialization.

Additionally if one or more of our product candidates receives marketing approval and we or others later identify undesirable side effects caused by such products, a number of potentially significant negative consequences could result, including:

- regulatory authorities may withdraw approvals of such product;
- regulatory authorities may require additional warnings on the label;
- we may be required to create a medication guide outlining the risks of such side effects for distribution to patients;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular peptide-based product candidate which could significantly harm our business and prospects.

We rely on third parties to conduct our pre-clinical studies and clinical trials. If these third parties do not successfully carry out their contractual duties or do not meet regulatory requirements or expected deadlines, we may not be able to obtain timely regulatory approval for or commercialize our product candidates and our business could be substantially harmed.

We have relied upon and plan to continue to rely upon third party CROs to monitor and manage clinical trials and collect data for our pre-clinical studies and clinical programs. We rely on these parties for execution of our pre-clinical studies and clinical trials, and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that their conduct meets regulatory requirements and that each of our studies and trials is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards, and our reliance on CROs does not relieve us of our regulatory responsibilities. Thus, we and our CROs are required to comply with good clinical practices (GCPs), which are regulations and guidelines promulgated by the FDA, the EMA and comparable foreign regulatory authorities for all of our product candidates in clinical development. Regulatory authorities enforce these GCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our CROs fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, EMA or comparable foreign regulatory authorities may

not accept the data or require us to perform additional clinical trials before considering our filing for regulatory approval or approving our marketing application. We cannot assure you that upon inspection by a regulatory authority, such regulatory authority will determine that any of our clinical trials complies with GCPs. While we have agreements governing activities of our CROs, we may have limited influence over their actual performance and the qualifications of their personnel conducting work on our behalf. In addition, significant portions of the clinical studies for our peptide-based product candidates are expected to be conducted outside of the US, which will make it more difficult for us to monitor CROs and perform visits of our clinical trial sites and will force us to rely heavily on CROs to ensure the proper and timely conduct of our clinical trials and compliance with applicable regulations, including GCPs. Failure to comply with applicable regulations in the conduct of the clinical studies for our peptide-based product candidates may require us to repeat clinical trials, which would delay the regulatory approval process.

Some of our CROs have an ability to terminate their respective agreements with us if it can be reasonably demonstrated that the safety of the subjects participating in our clinical trials warrants such termination, if we make a general assignment for the benefit of our creditors or if we are liquidated.

If any of our relationships with these third party CROs terminate, we may not be able to enter into arrangements with alternative CROs or do so on commercially reasonable terms. In addition, our CROs are not our employees, and except for remedies available to us under our agreements with such CROs, we cannot control whether or not they devote sufficient time and resources to our pre-clinical and clinical programs. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our peptide-based product candidates. As a result, our results of operations and the commercial prospects for our peptide-based product candidates would be harmed, our costs could increase substantially and our ability to generate revenue could be delayed significantly.

Switching or adding additional CROs involves additional cost and requires management time and focus. In addition, there is a natural transition period when a new CRO commences work. As a result, delays occur, which can materially impact our ability to meet our desired clinical development timelines. Though we carefully manage our relationships with our CROs, there can be no assurance that we will not encounter challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition and prospects.

We rely completely on third parties to manufacture our drug substance and clinical drug product and we intend to rely on third parties to produce commercial supplies of any approved peptide-based product candidate.

Our clinical trials must be conducted with product manufactured under cGMP and for Europe and other major countries, International Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) guidelines, and we rely on contract manufactures to manufacture and provide product for us that meet these requirements. We do not currently have nor do we plan to acquire the infrastructure or capability internally to manufacture our pre-clinical and clinical drug supplies and we lack the resources and the capability to manufacture any of our peptide-based product candidates on a clinical or commercial scale. We expect to continue to depend on contract manufacturers for the foreseeable future. In addition, we have no control over the ability of our contract manufacturers to maintain adequate quality control, quality assurance and qualified personnel. Moreover, our contract manufacturers are the sole source of supply for our clinical product candidates, including PTG-100. If we were to experience an unexpected loss of supply for any reason, whether as a result of manufacturing, supply or storage issues or otherwise, we could experience delays, disruptions, suspensions or termination of our clinical study and planned development program, or be required to restart or repeat, any ongoing clinical trials.

We also rely on our contract manufacturers to purchase from third party suppliers the materials necessary to produce our peptide-based product candidates for our clinical trials. There are a limited number of suppliers for raw materials that we use to manufacture our drugs and there may be a need to assess alternate suppliers to prevent a possible disruption of the manufacture of the materials necessary to produce our peptide-based product candidates for our clinical trials, and if approved, for commercial sale. We do not have any control over the process or timing of the acquisition of these raw materials by our manufacturers. Moreover, we currently do not have any agreements for the commercial production of these raw materials. Although we generally do not begin a clinical trial unless we believe we have a sufficient supply of a peptide-based product candidate to complete the clinical trial, any significant delay in the supply of a peptide-based product candidate, or the raw material components thereof, for an ongoing clinical trial due to the need to replace a contract manufacturer or other third party manufacturer could considerably delay completion of our clinical trials, product testing and potential regulatory approval of our peptide-based product candidates. If our contract manufacturers or we are unable to purchase these raw materials after regulatory approval has been obtained for our peptide-based product candidates, the commercial launch of our peptide-based product candidates would be delayed or there would be a shortage in supply, which would impair our ability to generate revenue from the sale of our peptide-based product candidates.

If we submit an application for regulatory approval of any of our product candidates, the facilities used by our contract manufacturers to manufacture our product candidates will be subject to inspection and approval by the FDA or other regulatory authorities. If our contract manufacturers cannot successfully manufacture material that conforms to our specifications and the strict regulatory requirements of the FDA or others, they will not be able to secure and/or maintain regulatory approval for their manufacturing facilities. If the FDA or a comparable foreign regulatory authority does not approve these facilities for the manufacture of our peptide-based product candidates or if it withdraws any such approval in the future, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our peptide-based product candidates, if approved.

We may fail to obtain orphan drug designations from the FDA for our product candidates, as applicable, and even if we obtain such designations, we may be unable to maintain the benefits associated with orphan drug designation, including the potential for market exclusivity.

Our strategy includes filing for orphan drug designation where available for our product candidates. Under the Orphan Drug Act, the FDA may grant orphan drug designation to a drug or biologic intended to treat a rare disease or condition, which is defined as one occurring in a patient population of fewer than 200,000 in the United States, or a patient population greater than 200,000 in the United States where there is no reasonable expectation that the cost of developing the drug or biologic will be recovered from sales in the United States. In the United States, orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. In addition, if a product that has orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan drug exclusivity, which means that the FDA may not approve any other applications, including a full NDA or BLA, to market the same drug or biologic for the same indication for seven years, except in limited circumstances, such as a showing of clinical superiority to the product with orphan drug exclusivity or where the manufacturer is unable to assure sufficient product quantity.

We have not obtained nor have we sought to obtain orphan designation for any product candidates to date, although we believe some of the potential indications of our product candidates could qualify for orphan drug designation and the related benefits if approved for that indication. For example, if PTG-100 or PTG-200 is developed for the treatment of pediatric IBD or PTG-300 for the treatment of iron overload disorders in patients with transfusion-dependent β-Thalassemia and possibly HH and SCD, we plan to file and expect to qualify for orphan drug designation with respect to such indication. Even if we obtain such designations, we may not be the first to obtain regulatory approval of a product candidate for the orphan-designated indication due to the uncertainties associated with developing pharmaceutical products. In addition, exclusive marketing rights in the

United States may be limited if we seek approval for an indication broader than the orphan-designated indication or may be lost if the FDA later determines that the request for designation was materially defective or if we are unable to assure sufficient quantities of the product to meet the needs of patients with the orphan-designated disease or condition. Further, even if we obtain orphan drug designation exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs with different active moieties may receive and be approved for the same condition, and only the first applicant to receive approval will receive the benefits of marketing exclusivity. Even after an orphan-designated product is approved, the FDA can subsequently approve a later drug with the same active moiety for the same condition if the FDA concludes that the later drug is clinically superior if it is shown to be safer, more effective or makes a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a drug, nor gives the drug any advantage in the regulatory review or approval process. In addition, while we may seek orphan drug designation for our product candidates, we may never receive such designations.

We may not be successful in obtaining or maintaining development and commercialization collaborations, and any potential partner may not devote sufficient resources to the development or commercialization of our product candidates or may otherwise fail in development or commercialization efforts, which could adversely affect our ability to develop certain of our product candidates and our financial condition and operating results.

We have no current collaborations for any of our product candidates. Even if we are able to establish collaboration arrangements, any such collaboration may not ultimately be successful, which could have a negative impact on our business, results of operations, financial condition and growth prospects. While we currently plan to enter into collaborations that are limited to certain identified territories, there can be no assurance that we would maintain significant rights or control of future development and commercialization of such product candidate. Accordingly, if we collaborate with a third party for development and commercialization of a product candidate, we may relinquish some or all of the control over the future success of that product candidate to the third party, and that partner may not devote sufficient resources to the development or commercialization of our product candidate or may otherwise fail in development or commercialization efforts, in which event the development and commercialization of the product candidate in the collaboration could be delayed or terminated and our business could be substantially harmed. In addition, the terms of any potential collaboration or other arrangement that we may establish may not be favorable to us or may not be perceived as favorable, which may negatively impact the price of our common stock. In some cases, we may be responsible for continuing development of a product candidate or research program under a collaboration, and the payments we receive from our partner may be insufficient to cover the cost of this development or may result in a dispute between the parties. Moreover, collaborations and sales and marketing arrangements are complex and time consuming to negotiate, document and implement and they may require substantial resources to maintain, which may be detrimental to the development of our other product candidates.

We are subject to a number of additional risks associated with our dependence on collaborations with third parties, the occurrence of which could cause our collaboration arrangements to fail. Conflicts may arise between us and partners, such as conflicts concerning the implementation of development plans, efforts and resources dedicated to the product candidate, interpretation of clinical data, the achievement of milestones, the interpretation of financial provisions or the ownership of intellectual property developed during the collaboration. If any such conflicts arise, a collaborator could act in its own self-interest, which may be adverse to our interests. Any such disagreement between us and a partner could result in one or more of the following, each of which could delay or prevent the development or commercialization of our product candidates, and in turn prevent us from generating sufficient revenue to achieve or maintain profitability:

- reductions in the payment of royalties or other payments we believe are due pursuant to the applicable collaboration arrangement;
- actions taken by a partner inside or outside our collaboration which could negatively impact our rights or benefits under our collaboration; or

- unwillingness on the part of a partner to keep us informed regarding the progress of its development and commercialization activities or to permit public disclosure of the results of those activities.

In addition, the termination of a collaboration may limit our ability to obtain rights to the product or intellectual property developed by our collaborator under terms that would be sufficiently favorable for us to consider further development or investment in the terminated collaboration product candidate, even if it were returned to us.

We face significant competition from other biotechnology and pharmaceutical companies, and our operating results will suffer if we fail to compete effectively.

The biotechnology and pharmaceutical industries are intensely competitive and subject to rapid and significant technological change. We have competitors worldwide, including major multinational pharmaceutical companies, biotechnology companies, specialty pharmaceutical and generic pharmaceutical companies as well as universities and other research institutions.

Many of our competitors have substantially greater financial, technical and other resources, such as larger research and development staff, and experienced marketing and manufacturing organizations. Mergers and acquisitions in our industry may result in even more resources being concentrated in our competitors. As a result, these companies may obtain regulatory approval more rapidly than we are able and may be more effective in selling and marketing their products. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies. Competition may increase further as a result of advances in the commercial applicability of newer technologies and greater availability of capital for investment in these industries. Our competitors may succeed in developing, acquiring or licensing, on an exclusive basis, pharmaceutical products that are easier to develop, more effective or less costly than any product candidates that we are currently developing or that we may develop. If approved, our product candidates are expected to face competition from commercially available drugs as well as drugs that are in the development pipelines of our competitors.

Pharmaceutical companies may invest heavily to accelerate discovery and development of novel compounds or to in-license novel compounds that could make our product candidates less competitive. In addition, any new product that competes with an approved product must demonstrate advantages in efficacy, convenience, tolerability or safety in order to overcome price competition and to be commercially successful. If our competitors succeed in obtaining FDA, EMA or other regulatory approval or discovering, developing and commercializing drugs before we do or develop blocking intellectual property to which we do not have a license, there would be a material adverse impact on the future prospects for our product candidates and business.

In particular, we believe our principal competition in the treatment of IBD will come from companies with approved agents in the following therapeutic classes, among others:

- Infused $\alpha 4\beta 7$ antibody: Takeda Pharmaceutical Company
- Infused IL-23 and IL-12 antibody: Johnson & Johnson Services (Stelara® BLA filed in moderate-to-severe CD)
- Injectable or infused TNF-α antibody: Abbvie, Johnson & Johnson, Roche, UCB S.A.

We are also aware of several companies developing therapeutic product candidates for the treatment of IBD, including, but not limited to AstraZeneca, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene (mongersen sodium and ozanimod hydrochloride in Phase 3 clinical trials), Encycle Therapeutics, Genentech (etrolizumab in a Phase 3 clinical trial), Gilead Sciences (GS-5745 in a Phase 3 clinical trial), Pfizer (tofacitinib citrate in a Phase 3 clinical trial), and Roche.

We believe our principal competition in the treatment of iron overload disorders, such as β-Thalassemia, HH and SCD, will come from other pipeline products being developed by companies such as Acceleron

(luspatercept in a Phase 3 clinical trial), bluebird bio, Bristol-Myers Squibb, Emmaus Medical (glutamine in a Phase 3 clinical trial), Global Blood, La Jolla Pharmaceutical and Merganser Biotech, among others. We believe competition will also include approved iron chelation therapies that have been developed by Novartis and Apotex, among others.

We believe that our ability to successfully compete will depend on, among other things:

- the efficacy and safety of our product candidates, in particular compared to marketed products and products in late-stage development;
- the time it takes for our product candidates to complete clinical development and receive regulatory approval, if at all;
- the ability to commercialize and market any of our product candidates that receive regulatory approval;
- the price of our products, including in comparison to branded or generic competitors;
- whether coverage and adequate levels of reimbursement are available under private and governmental health insurance plans, including Medicare;
- the ability to protect intellectual property rights related to our product candidates;
- the ability to manufacture and sell commercial quantities of any of our product candidates that receive regulatory approval; and
- acceptance of any of our approved product candidates by physicians, payors and other healthcare providers.

Because our research approach depends on our proprietary technology platform, it may be difficult for us to continue to successfully compete in the face of rapid changes in technology. If we fail to continue to advance our technology platform, technological change may impair our ability to compete effectively and technological advances or products developed by our competitors may render our technologies or product candidates obsolete, less competitive or not economical.

We currently have no marketing and sales organization. To the extent any of our peptide-based product candidates for which we maintain commercial rights is approved for marketing, if we are unable to establish marketing and sales capabilities or enter into agreements with third parties to market and sell our peptide-based product candidates, we may not be able to effectively market and sell any peptide-based product candidates, or generate product revenue.

We currently do not have a marketing or sales organization for the marketing, sales and distribution of pharmaceutical products. In order to commercialize any peptide-based product candidates that receive marketing approval, we would have to build marketing, sales, distribution, managerial and other non-technical capabilities or make arrangements with third parties to perform these services, and we may not be successful in doing so. In the event of successful development of any of our product candidates, we may elect to build a targeted specialty sales force which will be expensive and time consuming. Any failure or delay in the development of our internal sales, marketing and distribution capabilities would adversely impact the commercialization of these products. With respect to our peptide-based product candidates, we may choose to partner with third parties that have direct sales forces and established distribution systems, either to augment our own sales force and distribution systems or in lieu of our own sales force and distribution systems. If we are unable to enter into collaborations with third parties for the commercialization of approved products, if any, on acceptable terms or at all, or if any such partner does not devote sufficient resources to the commercialization of our product or otherwise fails in commercialization efforts, we may not be able to successfully commercialize any of our peptide-based product candidates that receive regulatory approval. If we are not successful in commercializing our peptide-based

product candidates, either on our own or through collaborations with one or more third parties, our future revenue will be materially and adversely impacted.

Even if our peptide-based product candidates receive marketing approval, they may fail to achieve market acceptance by physicians, patients, government payors (including Medicare and Medicaid programs), private insurers, and other third-party payors, or others in the medical community necessary for commercial success.

If any of our peptide-based product candidates receive marketing approval, they may nonetheless fail to gain sufficient market acceptance by physicians, patients, government payors, other third-party payors and other healthcare providers. If any of our approved peptide-based products fail to achieve an adequate level of acceptance, we may not generate significant revenue to become profitable. The degree of market acceptance, if approved for commercial sale, will depend on a number of factors, including but not limited to:

- the efficacy and potential advantages compared to alternative treatments;
- effectiveness of sales and marketing efforts;
- the cost of treatment in relation to alternative treatments;
- our ability to offer our peptide-based product candidates for sale at competitive prices;
- the convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the willingness of the medical community to offer customers our peptide-based product candidates in addition to or in the place of current injectable therapies;
- the strength of marketing and distribution support;
- the availability of government and third-party coverage and adequate reimbursement;
- the prevalence and severity of any side effects; and
- any restrictions on the use of our product candidates together with other medications.

Because we expect sales of our peptide-based product candidates, if approved, to generate revenue for us to achieve profitability, the failure of our peptide-based product candidates to achieve market acceptance would harm our business and could require us to seek collaborations or undertake additional financings sooner than we would otherwise plan.

We have focused our limited resources to pursue particular product candidates and indications, and consequently, we may fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we have focused on research programs and product candidates on the discovery and development of GI-restricted drugs that target the same biological pathways as currently marketed injectable antibody drugs for the treatment of IBD. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Our spending on current and future research and development programs and product candidates for specific indications may not yield any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration partnerships, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate.

Even if we obtain and maintain approval for any of our product candidates from the FDA, we may never obtain approval for our product candidates outside of the United States, which would limit our market opportunities and adversely affect our business.

Sales of our product candidates outside of the United States will be subject to foreign regulatory requirements governing clinical trials and marketing approval and, to the extent that we retain commercial rights following clinical development, we would plan to seek regulatory approval to commercialize our peptide-based product candidates in the United States, the EU and additional foreign countries. Even if the FDA grants marketing approval for a product candidate, comparable regulatory authorities of foreign countries must also approve the manufacturing and marketing of the product candidates in those countries. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from, and greater than, those in the US, including additional pre-clinical studies or clinical trials. In many countries outside the US, a product candidate must be approved for reimbursement before it can be approved for sale in that country. In some cases, the price that we intend to charge for our products is also subject to approval. We may decide to submit an MAA to the EMA for approval in the EEA. As with the FDA, obtaining approval of an MAA from the EMA is a similarly lengthy and expensive process and the EMA has its own procedures for approval of peptide-based product candidates. Even if a product is approved, the FDA or the EMA, as the case may be, may limit the indications for which the product may be marketed, require extensive warnings on the product labeling or require expensive and time-consuming clinical trials or reporting as conditions of approval. Regulatory authorities in countries outside of the US and the EEA also have requirements for approval of drug candidates with which we must comply prior to marketing in those countries. Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our products in certain countries. Further, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries and regulatory approval in one country does not ensure approval in any other country, while a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory approval process in others. Also, regulatory approval for any of our peptide-based product candidates may be withdrawn. If we fail to comply with the regulatory requirements in international markets and or receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our peptide-based product candidates will be harmed and our business will be adversely affected.

If we fail to comply with state and federal healthcare regulatory laws, we could face substantial penalties, damages, fines, disgorgement, exclusion from participation in governmental healthcare programs, and the curtailment of our operations, any of which could adversely affect our business, operations, and financial condition.

Healthcare providers, physicians and third-party payors will play a primary role in the recommendation and prescription of any future product candidates we may develop any product candidates for which we obtain marketing approval. Our arrangements with third-party payors and customers may expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may affect the business or financial arrangements and relationships through which we would market, sell and distribute our products. Even though we do not and will not control referrals of healthcare services or bill directly to Medicare, Medicaid or other third-party payors, federal and state healthcare laws and regulations pertaining to fraud and abuse and patients' rights are and will be applicable to our business. The laws that may affect our ability to operate include, but are not limited to:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, receiving, offering, or paying remuneration, directly or indirectly, in cash or in kind, in exchange for or to induce either the referral of an individual for, or the purchase, lease, order or recommendation of, any good, facility, item or service for which payment may be made, in whole or in part, under a federal healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation;

- the federal false claims and civil monetary penalties laws, including the False Claims Act, which impose criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false, fictitious, or fraudulent; knowingly making using, or causing to be made or used, a false record or statement to get a false or fraudulent claim paid or approved by the government; or knowingly making, using, or causing to be made or used, a false record or statement to avoid, decrease or conceal an obligation to pay money to the federal government; in addition, the government may assert that a claim including items and services resulting from a violation of the federal Anti-Kickback Statute constitutes a false of fraudulent claim for purposes of the False Claims Act;

- the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA), which imposes additional criminal and civil liability for, among other things, willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or making false or fraudulent statements relating to healthcare matters; similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act (HITECH), and their implementing regulations, which also imposes obligations, including mandatory contractual terms, on certain types of people and entities with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

- the federal civil monetary penalties statute, which prohibits, among other things, the offering or giving of remuneration to a Medicare or Medicaid beneficiary that the person knows or should know is likely to influence the beneficiary's selection of a particular supplier of items or services reimbursable by a Federal or state governmental program;

- the federal Physician Payment Sunshine Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to the government information related to certain payments and other "transfers of value" made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, and requires applicable manufacturers to report annually to the government ownership and investment interests held by the physicians described above and their immediate family members and payments or other "transfers of value" to such physician owners; and

- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by any third-party payor, including commercial insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; and state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; and state and foreign laws governing the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Further, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act (collectively, the ACA), among other things, amended the intent requirements of the federal Anti-Kickback Statute and certain criminal statutes governing healthcare fraud. A person or entity can now be found guilty of violating the statute without actual knowledge of the statute or specific intent to violate it. In addition, ACA provided that the government may assert that a claim including items or services resulting from a

violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act. Moreover, while we do not submit claims and our customers make the ultimate decision on how to submit claims, from time to time, we may provide reimbursement guidance to our customers. If a government authority were to conclude that we provided improper advice to our customers or encouraged the submission of false claims for reimbursement, we could face action against us by government authorities. Any violations of these laws, or any action against us for violation of these laws, even if we successfully defend against it, could result in a material adverse effect on our reputation, business, results of operations and financial condition.

We have entered into consulting and scientific advisory board arrangements with physicians and other healthcare providers, including some who could influence the use of our product candidates, if approved. While we have worked to structure our arrangements to comply with applicable laws, because of the complex and far-reaching nature of these laws, regulatory agencies may view these transactions as prohibited arrangements that must be restructured, or discontinued, or for which we could be subject to other significant penalties. We could be adversely affected if regulatory agencies interpret our financial relationships with providers who may influence the ordering of and use our product candidates, if approved, to be in violation of applicable laws.

The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and regulations. Federal and state enforcement bodies have recently increased their scrutiny of interactions between healthcare companies and healthcare providers, which has led to a number of investigations, prosecutions, convictions and settlements in the healthcare industry. Responding to investigations can be time-and resource-consuming and can divert management's attention from the business. Additionally, as a result of these investigations, healthcare providers and entities may have to agree to additional onerous compliance and reporting requirements as part of a consent decree or corporate integrity agreement. Any such investigation or settlement could increase our costs or otherwise have an adverse effect on our business.

If our operations are found to be in violation of any of these laws or any other governmental laws and regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, disgorgement, imprisonment, exclusion from government funded healthcare programs, such as Medicare and Medicaid, disgorgement, contractual damages, reputational harm, diminished profits and the curtailment or restructuring of our operations. If any of the physicians or other healthcare providers or entities with whom we expect to do business is found to be not in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

Recently enacted and future legislation may increase the difficulty and cost for us to obtain marketing approval of and commercialize our product candidates and affect the prices we may obtain.

In the United States and some foreign jurisdictions, there have been, and we expect there will continue to be, a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could, among other things, prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any peptide-based product candidates for which we obtain marketing approval.

For example, in the United States in March 2010, the ACA was enacted to increase access to health insurance, reduce or constrain the growth of healthcare spending, enhance remedies against fraud and abuse, add new transparency requirements for health care and the health insurance industries, impose new taxes and fees on the health industry and impose additional health policy reforms. The law has continued the downward pressure on pharmaceutical pricing, especially under the Medicare program, and increased the industry's regulatory burdens and operating costs. Among the provisions of the ACA of importance to our potential peptide-based product candidates are the following:

- an annual, non-tax deductible fee payable by any entity that manufactures or imports specified branded prescription drugs and biologic agents payable to the federal government based on each company's market share of prior year total sales of branded products to certain federal healthcare programs;

- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- extension of manufacturers' Medicaid rebate liability to individuals enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs in certain states;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries under their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;
- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

The financial impact of the ACA over the next few years will depend on a number of factors including but not limited to the policies reflected in implementing regulations and guidance and changes in sales volumes for products affected by the new system of rebates, discounts and fees.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. These changes included aggregate reductions to Medicare payments to providers of 2% per fiscal year, which went into effect in April 2013 and, due to subsequent legislative amendments to the statute, will remain in effect through 2025 unless additional action is taken by Congress. In January 2013, the American Taxpayer Relief Act of 2012 was signed into law, which, among other things, further reduced Medicare payments to several types of providers and increased the statute of limitations period in which the government may recover overpayments to providers from three to five years. In addition, recently there has been heightened governmental scrutiny over the manner in which drug manufacturers set prices for their commercial products. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our product candidates, if approved.

We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare therapies, which could result in reduced demand for our peptide-based product candidates or additional pricing pressures.

Legislative and regulatory proposals have also been made to expand post-approval requirements and restrict sales and promotional activities for pharmaceutical products. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

Governments outside the United States tend to impose strict price controls, which may adversely affect our revenues, if any.

In some countries, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of

marketing approval for a product candidate. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels, including as part of cost containment measures. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after coverage and reimbursement have been obtained. Reference pricing used by various countries and parallel distribution or arbitrage between low-priced and high-priced countries, can further reduce prices. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies, which is time-consuming and costly. If coverage and reimbursement of our product candidates are unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed, possibly materially.

Our future success depends on our ability to retain our executive officers and to attract, retain and motivate qualified personnel. If we are not successful in attracting and retaining highly qualified personnel, we may not be able to successfully implement our business strategy.

Our industry has experienced a high rate of turnover of management personnel in recent years. Our ability to compete in the highly competitive biotechnology and pharmaceuticals industries depends upon our ability to attract and retain highly qualified managerial, scientific, medical and regulatory personnel. We are highly dependent on our existing senior management team, especially Dinesh V. Patel, Ph.D., our President and Chief Executive Officer, David Y. Liu, Ph.D., our Chief Scientific Officer and Head of Research and Development, Richard S. Shames, M.D., our Chief Medical Officer, Tom O'Neil, our Chief Financial Officer and William Hodder, our Senior Vice President of Corporate Development. We are not aware of any present intention of any of these individuals to leave us. In order to induce valuable employees to continue their employment with us, we have provided stock options that vest over time. The value to employees of stock options that vest over time is significantly affected by movements in our stock price that are beyond our control, and may at any time be insufficient to maintain retention incentives or counteract more lucrative offers from other companies. All of our employees may terminate their employment with us at any time, with or without notice. The loss of the services of any of our executive officers or other key employees and our inability to find suitable replacements would harm our research and development efforts as well as our business, financial condition and prospects. Our success also depends on our ability to continue to attract, retain and motivate highly skilled and experienced personnel with scientific, medical, regulatory, manufacturing and management training and skills.

We may not be able to attract or retain qualified personnel in the future due to the intense competition for a limited number of qualified personnel among biopharmaceutical, biotechnology, pharmaceutical and other businesses. Many of the other biopharmaceutical and pharmaceutical companies that we compete against for qualified personnel have greater financial and other resources, different risk profiles and a longer history in the industry than we do. Our competitors may provide higher compensation or more diverse opportunities and better opportunities for career advancement. Any or all of these competing factors may limit our ability to continue to attract and retain high quality personnel, which could negatively affect our ability to successfully develop and commercialize peptide-based product candidates and to grow our business and operations as currently contemplated.

We will need to expand the size of our organization, and we may experience difficulties in managing this growth.

As of June 30, 2016, we had 29 full-time employees. As our development and commercialization plans and strategies develop and operate as a public company, we expect to need additional managerial, operational, scientific, sales, marketing, development, regulatory, manufacturing, financial and other resources. Future growth would impose significant added responsibilities on members of management, including:

- designing and managing our clinical trials effectively;
- identifying, recruiting, maintaining, motivating and integrating additional employees;

- managing our manufacturing and development efforts effectively;
- improving our managerial, development, operational and financial systems and controls; and
- expanding our facilities.

As our operations expand, we expect that we will need to manage relationships with strategic collaborators, CROs, contract manufacturers, suppliers, vendors and other third parties. Our future financial performance and our ability to develop and commercialize our peptide-based product candidates and to compete effectively will depend, in part, on our ability to manage any future growth effectively. We may not be successful in accomplishing these tasks in growing our company, and our failure to accomplish any of them could adversely affect our business and operations.

Significant disruptions of information technology systems or breaches of data security could adversely affect our business.

Our business is increasingly dependent on critical, complex and interdependent information technology systems, including Internet-based systems, to support business processes as well as internal and external communications. The size and complexity of our internal computer systems and those of our CROs, contract manufacturers and other third parties on which we relay make them potentially vulnerable to breakdown, telecommunications and electrical failures, malicious intrusion and computer viruses that may result in the impairment of key business processes. In addition, our systems are potentially vulnerable to data security breaches—whether by employees or others—that may expose sensitive data to unauthorized persons. Such data security breaches could lead to the loss of trade secrets or other intellectual property, or could lead to the public exposure of personally identifiable information (including sensitive personal information) of our employees, collaborators, clinical trial patients, and others. A data security breach or privacy violation that leads to disclosure or modification of or prevents access to patient information, including personally identifiable information or protected health information, could harm our reputation, compel us to comply with federal and/or state breach notification laws, subject us to mandatory corrective action, require us to verify the correctness of database contents and otherwise subject us to liability under laws and regulations that protect personal data, resulting in increased costs or loss of revenue. If we are unable to prevent such data security breaches or privacy violations or implement satisfactory remedial measures, our operations could be disrupted, and we may suffer loss of reputation, financial loss and other regulatory penalties because of lost or misappropriated information, including sensitive patient data. In addition, these breaches and other inappropriate access can be difficult to detect, and any delay in identifying them may lead to increased harm of the type described above. Moreover, the prevalent use of mobile devices that access confidential information increases the risk of data security breaches, which could lead to the loss of confidential information, trade secrets or other intellectual property. While we have implemented security measures to protect our data security and information technology systems, such measures may not prevent such events. Any such disruptions and breaches of security could have a material adverse effect on the development of our product candidates as well as our business and financial condition.

Our insurance policies are expensive and only protect us from some business risks, which will leave us exposed to significant uninsured liabilities.

We do not carry insurance for all categories of risk that our business may encounter. Some of the policies we currently maintain include general liability, employment practices liability, property, auto, workers' compensation, products liability and directors' and officers' insurance. We do not know, however, if we will be able to maintain insurance with adequate levels of coverage. Any significant uninsured liability may require us to pay substantial amounts, which would adversely affect our financial position and results of operations.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could have a material adverse effect on the success of our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials or other work-related injuries, this insurance may not provide adequate coverage against potential liabilities. In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Our employees, independent contractors, principal investigators, consultants and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements, which could have a material adverse effect on our business.

We are exposed to the risk that our employees, independent contractors, principal investigators, consultants and vendors may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or disclosure of unauthorized activities to us that violates: (i) FDA laws and regulations or those of comparable foreign regulatory authorities, including those laws that require the reporting of true, complete and accurate information to the FDA, (ii) manufacturing standards, (iii) federal and state data privacy, security, fraud and abuse and other healthcare laws and regulations established and enforced by comparable foreign regulatory authorities, or (iv) laws that require the true, complete and accurate reporting of financial information or data. Activities subject to these laws also involve the improper use or misrepresentation of information obtained in the course of clinical trials, creating fraudulent data in our pre-clinical studies or clinical trials or illegal misappropriation of drug product, which could result in regulatory sanctions and cause serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and third-parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. Additionally, we are subject to the risk that a person or government could allege such fraud or other misconduct, even if none occurred. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant fines or other sanctions.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of any of our peptide-based product candidates, if approved.

We face an inherent risk of product liability as a result of the clinical testing of our peptide-based product candidates and will face an even greater risk if we commercialize any products. For example, we may be sued if any product we develop allegedly causes injury or is found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product, negligence, strict liability and a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required

to stop development or, if approved, limit commercialization of our peptide-based product candidates. Even successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- delay or termination of clinical studies;
- injury to our reputation;
- withdrawal of clinical trial participants;
- initiation of investigations by regulators;
- costs to defend the related litigation;
- a diversion of management's time and our resources;
- substantial monetary awards to trial participants or patients;
- decreased demand for our peptide-based product candidates;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenue from product sales; and
- the inability to commercialize any our peptide-based product candidates, if approved.

Our inability to obtain and retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the development or commercialization of our peptide-based product candidates. We currently carry $7.7 million in clinical trial liability insurance, which we believe is appropriate for our clinical trials. Although we maintain such insurance, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. Our insurance policies also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We will have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts.

We currently conduct, and intend to continue to conduct a substantial portion of the clinical trials for our product candidates outside of the United States. If approved, we may commercialize our product candidates abroad. We will thus be subject to the risks of doing business outside of the United States.

We currently conduct, and intend to continue to conduct, a substantial portion of our clinical trials outside of the United States and, if approved, we intend to also market our peptide-based product candidates outside of the United States. We are thus subject to risks associated with doing business outside of the United States. With respect to our peptide-based product candidates, we may choose to partner with third parties that have direct sales forces and established distribution systems, either to augment our own sales force and distribution systems outside of the United States or in lieu of our own sales force and distribution systems, which would indirectly expose us to these risks. Our business and financial results in the future could be adversely affected due to a variety of factors associated with conducting development and marketing of our peptide-based product candidates, if approved, outside of the United States, including:

- Medical standard of care and diagnostic criteria may differ in foreign jurisdictions, which may impact our ability to enroll and successfully complete trials designed for U.S. marketing;
- efforts to develop an international sales, marketing and distribution organization may increase our expenses, divert our management's attention from the acquisition or development of peptide-based product candidates or cause us to forgo profitable licensing opportunities in these geographies;
- changes in a specific country's or region's political and cultural climate or economic condition;

- unexpected changes in foreign laws and regulatory requirements;
- difficulty of effective enforcement of contractual provisions in local jurisdictions;
- inadequate intellectual property protection in foreign countries;
- trade-protection measures, import or export licensing requirements such as Export Administration Regulations promulgated by the US Department of Commerce and fines, penalties or suspension or revocation of export privileges;
- regulations under the U.S. Foreign Corrupt Practices Act and similar foreign anti-corruption laws;
- the effects of applicable foreign tax structures and potentially adverse tax consequences; and
- significant adverse changes in foreign currency exchange rates which could make the cost of our clinical trials, to the extent conducted outside of the US, more expensive.

Our headquarters and certain of our data storage facilities are located near known earthquake fault zones. The occurrence of an earthquake, fire or any other catastrophic event could disrupt our operations or the operations of third parties who provide vital support functions to us, which could have a material adverse effect on our business and financial condition.

We and some of the third party service providers on which we depend for various support functions, such as data storage, are vulnerable to damage from catastrophic events, such as power loss, natural disasters, terrorism and similar unforeseen events beyond our control. Our corporate headquarters and other facilities are located in the San Francisco Bay Area, which in the past has experienced severe earthquakes and fires.

We do not carry earthquake insurance. Earthquakes or other natural disasters could severely disrupt our operations, and have a material adverse effect on our business, results of operations, financial condition and prospects.

If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our headquarters, damaged critical infrastructure, such as our data storage facilities or financial systems, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. We do not have a disaster recovery and business continuity plan in place. We may incur substantial expenses as a result of the absence or limited nature of our internal or third party service provider disaster recovery and business continuity plans, which, particularly when taken together with our lack of earthquake insurance, could have a material adverse effect on our business. Furthermore, integral parties in our supply chain are operating from single sites, increasing their vulnerability to natural disasters or other sudden, unforeseen and severe adverse events. If such an event were to affect our supply chain, it could have a material adverse effect on our development plans and business.

The insurance coverage and reimbursement status of newly-approved products is uncertain. Failure to obtain or maintain adequate coverage and reimbursement for our peptide-based product candidates could limit our ability to generate revenue.

The availability and extent of reimbursement by governmental and private payors is essential for most patients to be able to afford medications and therapies. Sales of any of our peptide-based product candidates that receive marketing approval will depend substantially, both in the United States and internationally, on the extent to which the costs of our peptide-based product candidates will be paid by health maintenance, managed care, pharmacy benefit and similar healthcare management organizations, or reimbursed by government health administration authorities, private health coverage insurers and other third-party payors. If reimbursement is not available, or is available only to limited levels, we may not be able to successfully commercialize our product candidates. Even if coverage is provided, the approved reimbursement amount may not be high enough to allow us to establish or maintain adequate pricing that will allow us to realize a sufficient return on our investment.

There is significant uncertainty related to the insurance coverage and reimbursement of newly approved products. In the United States, the principal decisions about reimbursement for new products are typically made by the Centers for Medicare & Medicaid Services (CMS), an agency within the United States Department of Health and Human Services. CMS decides whether and to what extent a new product will be covered and reimbursed under Medicare. Private payors tend to follow CMS to a substantial degree. It is difficult to predict what CMS will decide with respect to reimbursement for novel products such as ours since there is no body of established practices and precedents for these new products. Reimbursement agencies in Europe may be more conservative than CMS.

Outside the United States, international operations are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe, Canada and other countries may cause us to price our tablet vaccine candidates on less favorable terms that we currently anticipate. In many countries, particularly the countries of the European Union, the prices of medical products are subject to varying price control mechanisms as part of national health systems. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our peptide-based product candidates to other available therapies. In general, the prices of products under such systems are substantially lower than in the United States. Other countries allow companies to fix their own prices for products, but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our peptide-based product candidates. Accordingly, in markets outside the United States, the reimbursement for our products may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenues and profits.

Moreover, increasing efforts by governmental and third-party payors, in the United States and internationally, to cap or reduce healthcare costs may cause such organizations to limit both coverage and level of reimbursement for new products approved and, as a result, they may not cover or provide adequate payment for our product candidates. We expect to experience pricing pressures in connection with the sale of any of our tablet vaccine candidates due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative changes. The downward pressure on healthcare costs in general, particularly prescription drugs and surgical procedures and other treatments, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products into the healthcare market.

Risks Related to Our Intellectual Property

If we are unable to obtain or protect intellectual property rights related to our product candidates and technologies, we may not be able to compete effectively in our markets.

We rely upon a combination of patent protection, trade secret protection and confidentiality agreements to protect the intellectual property related to our product candidates and technologies. The strength of patents in the biotechnology and pharmaceutical field involves complex legal and scientific questions and can be uncertain. The patent prosecution process is expensive and time-consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost, in a timely manner, or in all jurisdictions. The patent applications that we own or license may fail to result in issued patents in the United States or in other foreign countries, or they may fail to result in issued patents with claims that cover our product candidates or technologies in the United States or in other foreign countries. There is no assurance that all the potentially relevant prior art relating to our patent and patent applications has been found, which can invalidate a patent or prevent a patent from issuing from a pending patent application. Even if patents have been issued, or do successfully issue, from our patent applications, third parties may challenge the validity, enforceability or scope thereof, which may result in such patents being narrowed, invalidated or held unenforceable. Furthermore, even if they are unchallenged, our patent and patent applications may not adequately protect our intellectual property, provide exclusivity for our product candidates and technologies, or prevent others from designing around our claims.

If the breadth or strength of protection provided by the patent and patent applications we hold, obtain or pursue with respect to our product candidates and technologies is challenged, or if they fail to provide meaningful exclusivity for our product candidates and technologies, it could threaten our ability to commercialize our product candidates and technologies. Several patent applications covering our product candidates and technologies have been filed recently. We cannot offer any assurances about which, if any, patents will issue, the breadth of any such patent, or whether any issued patents will be found invalid and unenforceable or will be threatened by third parties. Any successful opposition to these patents or any other patents owned by or, if applicable in the future, licensed to us could deprive us of rights necessary for the successful commercialization of any product candidates and technologies that we may develop. Further, if we encounter delays in our clinical trials or in gaining regulatory approval, the period of time during which we could market any of our product candidates under patent protection, if approved, would be reduced. Since patent applications in the United States and most other countries are confidential for a period of time after filing, we cannot be certain that we or our licensors were the first to file any patent application related to our product candidates and technologies. Furthermore, an interference proceeding can be provoked by a third party or instituted by the U.S. Patent and Trademark Office (PTO) to determine who was the first to invent any of the subject matter covered by the patent claims of our applications. In addition, patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after it is filed. Various extensions may be available however the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired for a product, we may be open to competition from generic medications.

If, in the future, we obtain licenses from third parties, in some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications or to maintain any patents, covering technology that we license from third parties. We may also require the cooperation of our licensors to enforce any licensed patent rights, and such cooperation may not be provided. Therefore, these patents and applications may not be prosecuted and enforced in a manner consistent with the best interests of our business. Moreover, if we do obtain necessary licenses, we will likely have obligations under those licenses, and any failure to satisfy those obligations could give our licensor the right to terminate the license. Termination of a necessary license could have a material adverse impact on our business.

If we are unable to protect the confidentiality of our trade secrets and proprietary know-how or if competitors independently develop viable competing products, our business and competitive position may be harmed.

While we hold one issued patent and have filed patent applications to protect certain aspects of our product candidates, we also rely on trade secret protection and confidentiality agreements to protect proprietary scientific, business and technical information and know-how that is not or may not be patentable or that we elect not to patent. For example, we primarily rely on trade secrets and confidentiality agreements to protect our peptide therapeutics technology platform. Any disclosure to or misappropriation by third parties of our confidential proprietary information could enable competitors to quickly duplicate or surpass our technological achievements, thus eroding our competitive position in our market.

We seek to protect our proprietary information, data and processes, in part, by confidentiality agreements and invention assignment agreements with our employees, consultants, scientific advisors, contractors and partners. Although these agreements are designed to protect our proprietary information, we cannot be certain that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques. Although we require all of our employees to assign their inventions to us, and endeavor to execute confidentiality agreements with all of our employees, consultants, advisors and any third parties who have access to our proprietary know-how and other confidential information related to such technology, we cannot be certain that we have executed such agreements with all third parties who may have helped to develop our intellectual property or who had access to our proprietary information, nor can be we certain that our agreements will not be breached. If any of the parties to these confidentiality agreements breaches or violates the terms of such agreements, we may not have adequate remedies for any such breach or violation, and we could lose our trade secrets as a result.

We also seek to preserve the integrity and confidentiality of our data, trade secrets and know-how by maintaining physical security of our premises and physical and electronic security of our information technology systems. Monitoring unauthorized uses and disclosures is difficult, and we do not know whether the steps we have taken to protect our proprietary technologies will be effective. We cannot guarantee that our trade secrets and other proprietary and confidential information will not be disclosed or that competitors will not otherwise gain access to our trade secrets.

Enforcing a claim that a third party illegally obtained and is using our trade secrets, like patent litigation, is expensive and time-consuming, and the outcome is unpredictable. Further, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. The enforceability of confidentiality agreements may vary from jurisdiction to jurisdiction. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and abroad. Additionally, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating the trade secret. We cannot guarantee that our employees, former employees or consultants will not file patent applications claiming our inventions. Because of the "first-to-file" laws in the United States, such unauthorized patent application filings may defeat our attempts to obtain patents on our own inventions.

Trade secrets and know-how can be difficult to protect as trade secrets and know-how will over time be disseminated within the industry through independent development, the publication of journal articles, and the movement of personnel skilled in the art from company to company or academic to industry scientific positions. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent such competitor from using that technology or information to compete with us, which could harm our competitive position. If we are unable to prevent material disclosure of the intellectual property related to our technologies to third parties, we will not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, results of operations and financial condition.

Even if we are able to adequately protect our trade secrets and proprietary information, our trade secrets could otherwise become known or could be independently discovered by our competitors. Competitors could purchase our products and attempt to replicate some or all of the competitive advantages we derive from our development efforts, willfully infringe our intellectual property rights, design around our protected technology or develop their own competitive technologies that fall outside of our intellectual property rights. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, in the absence of patent protection, we would have no right to prevent them, or those to whom they communicate, from using that technology or information to compete with us. If our trade secrets are not adequately protected so as to protect our market against competitors' products, others may be able to exploit our proprietary peptide product candidate discovery technologies to identify and develop competing product candidates, and thus our competitive position could be adversely affected, as could our business.

We may be involved in lawsuits to protect or enforce our intellectual property, which could be expensive, time consuming and unsuccessful.

Competitors may infringe our issued patent or any patents issued as a result of our pending or future patent applications. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that a patent of ours is not valid or is unenforceable, or may refuse to stop the other party in such infringement proceeding from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated, held unenforceable or interpreted narrowly, and could put any of our patent applications at risk of not yielding an issued patent.

Interference proceedings provoked by third parties or brought by us, the PTO or any foreign patent authority may be necessary to determine the priority of inventions with respect to our patent or patent applications. An

unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms, if any license is offered at all. Our defense of litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees.

We may not be able to prevent misappropriation of our intellectual property, trade secrets or confidential information, particularly in countries where the laws may not protect those rights as fully as in the United States. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock.

Any issued patents covering our product candidates, including any patent that may issue from as a result of our pending or future patent applications, could be found invalid or unenforceable if challenged in court in the United States or abroad.

If we initiate legal proceedings against a third party to enforce a patent covering our product candidates or technologies, the defendant could counterclaim that such patent is invalid or unenforceable. In patent litigation in the U.S., defendant counterclaims alleging invalidity or unenforceability are commonplace, and there are numerous grounds upon which a third party can assert invalidity or unenforceability of a patent. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the PTO, or made a misleading statement, during prosecution. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, inter partes review, post grant review, and equivalent proceedings in foreign jurisdictions, such as opposition or derivation proceedings. Such proceedings could result in revocation or amendment to our patents in such a way that they no longer cover and protect our product candidates or technologies. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity of our patents, for example, we cannot be certain that there is no invalidating prior art of which we, our patent counsel, and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on our product candidates. Such a loss of patent protection could have a material adverse impact on our business.

The lives of any patents issued as a result of our pending or future patent applications may not be sufficient to effectively protect our products and business.

Patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after its first effective filing date. Although various extensions may be available, the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired for a product, we may be open to competition from generic medications. If patents are issued on our pending patent applications, the resulting patents are projected to expire on dates ranging from 2022 to 2035. In addition, although upon issuance in the United States the life of a patent can be increased based on certain delays caused by the USPTO, this increase can be reduced or eliminated based on certain delays caused by the patent applicant during patent prosecution. If we do not have sufficient patent life to protect our products, our business and results of operations will be adversely affected.

Competitors could enter the market with generic versions of our product candidates, which may result in a material decline in sales of our product candidates.

Under the Hatch-Waxman Act, a pharmaceutical manufacturer may file an abbreviated new drug application, or ANDA, seeking approval of a generic copy of an approved innovator product. Under the Hatch-Waxman Act, a manufacturer may also submit an NDA under section 505(b)(2) that references the FDA's finding of safety and effectiveness of a previously approved drug. A 505(b)(2) NDA product may be for a new or improved version of the original innovator product. Innovative small molecule drugs may be eligible for certain periods of regulatory exclusivity (e.g., five years for new chemical entities, three years for changes to an approved drug requiring a new clinical study, seven years for orphan drugs), which preclude FDA approval (or in some circumstances, FDA filing and review of) an ANDA or 505(b)(2) NDA relying on the FDA's finding of safety and effectiveness for the innovative drug. In addition to the benefits of regulatory exclusivity, an innovator NDA holder may have patents claiming the active ingredient, product formulation or an approved use of the drug, which would be listed with the product in the FDA publication, "Approved Drug Products with Therapeutic Equivalence Evaluations," known as the "Orange Book." If there are patents listed in the Orange Book, a generic applicant that seeks to market its product before expiration of the patents must include in the ANDA or 505(b)(2) what is known as a "Paragraph IV certification," challenging the validity or enforceability of, or claiming non-infringement of, the listed patent or patents. Notice of the certification must be given to the innovator, too, and if within 45 days of receiving notice the innovator sues to protect its patents, approval of the ANDA is stayed for 30 months, or as lengthened or shortened by the court.

Accordingly, if our product candidates are approved, competitors could file ANDAs for generic versions of our product candidates, or 505(b)(2) NDAs that reference our product candidates. If there are patents listed for our product candidates in the Orange Book, those ANDAs and 505(b)(2) NDAs would be required to include a certification as to each listed patent indicating whether the ANDA applicant does or does not intend to challenge the patent. We cannot predict whether any patents issuing from our pending patent applications will be eligible for listing in the Orange Book, how any generic competitor would address such patents, whether we would sue on any such patents, or the outcome of any such suit.

We may not be successful in securing or maintaining proprietary patent protection for products and technologies we develop or license. Moreover, if any patents that are granted and listed in the Orange Book are successfully challenged by way of a Paragraph IV certification and subsequent litigation, the affected product could more immediately face generic competition and its sales would likely decline materially. Should sales decline, we may have to write off a portion or all of the intangible assets associated with the affected product and our results of operations and cash flows could be materially and adversely affected.

Third party claims of intellectual property infringement may prevent or delay our drug discovery and development efforts.

Our commercial success depends in part on our ability to develop, manufacture, market and sell our drug candidates and use our proprietary technologies without infringing or otherwise violating the patents and proprietary rights of third parties. There is a substantial amount of litigation involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, derivation proceedings, post grant reviews, inter partes reviews, and reexamination proceedings before the PTO or oppositions and other comparable proceedings in foreign jurisdictions. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing product candidates, and there may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates and technologies. Third parties, including our competitors may initiate legal proceedings against us alleging that we are infringing or otherwise violating their patent or other intellectual property rights. Given the vast number of patents in our field of technology, we cannot assure you that marketing of our product candidates or practice of our technologies will not infringe existing patents or patents that may be

granted in the future. Because patent applications can take many years to issue and may be confidential for 18 months or more after filing, and because pending patent claims can be revised before issuance, there may be applications now pending of which we are unaware that may later result in issued patents that may be infringed by the practice of our peptide therapeutics technology platform or the manufacture, use or sale of our product candidates. If a patent holder believes our product candidates or technologies infringe on its patent, the patent holder may sue us even if we have received patent protection for our product candidates and technologies. In addition, third parties may obtain patents in the future and claim that our product candidates or technologies infringe upon these patents. If any third-party patents were held by a court of competent jurisdiction to cover the manufacturing process of any of our product candidates, any molecules formed during the manufacturing process or any final product or formulation itself, the holders of any such patents may be able to block our ability to commercialize such product candidate unless we obtained a license under the applicable patents, or until such patents expire. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates or technologies may give rise to claims of infringement of the patent rights of others.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further practice our technologies or develop and commercialize one or more of our product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. Even if we are successful in defending against any infringement claims, litigation is expensive and time-consuming and is likely to divert management's attention and substantial resources from our core business, which could harm our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement (which may include situations in which we had knowledge of an issued patent but nonetheless proceeded with activity which infringed such patent), limit our uses, pay royalties or redesign our infringing product candidates, which may be impossible or require substantial time and monetary expenditure. We may choose to seek, or may be required to seek, a license from the third-party patent holder and would most likely be required to pay license fees or royalties or both, each of which could be substantial. These licenses may not be available on commercially reasonable terms, however, or at all. Even if we were able to obtain a license, the rights we obtain may be nonexclusive, which would provide our competitors access to the same intellectual property rights upon which we are forced to rely. Furthermore, even in the absence of litigation, we may need to obtain licenses from third parties to advance our research or allow commercialization of our product candidates, and we have done so from time to time. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In such an event, we would be unable to further practice our technologies or develop and commercialize any of our product candidates at issue, which could harm our business significantly.

We may not identify relevant third party patents or may incorrectly interpret the relevance, scope or expiration of a third party patent which might adversely affect our ability to develop and market our products.

We cannot guarantee that any of our patent searches or analyses, including the identification of relevant patents, the scope of patent claims or the expiration of relevant patents, are complete or thorough, nor can we be certain that we have identified each and every third party patent and pending application in the United States and abroad that is relevant to or necessary for the commercialization of our product candidates in any jurisdiction.

The scope of a patent claim is determined by an interpretation of the law, the written disclosure in a patent and the patent's prosecution history. Our interpretation of the relevance or the scope of a patent or a pending application may be incorrect, which may negatively impact our ability to market our products. We may incorrectly determine that our products are not covered by a third party patent or may incorrectly predict whether a third party's pending application will issue with claims of relevant scope. Our determination of the expiration date of any patent in the United States or abroad that we consider relevant may be incorrect, which may negatively impact our ability to develop and market our product candidates. Our failure to identify and correctly interpret relevant patents may negatively impact our ability to develop and market our products.

Because of the expense and uncertainty of litigation, we may not be in a position to enforce our intellectual property rights against third parties.

Because of the expense and uncertainty of litigation, we may conclude that even if a third party is infringing our issued patent, any patents that may be issued on as a result of our pending or future patent applications or other intellectual property rights, the risk-adjusted cost of bringing and enforcing such a claim or action may be too high or not in the best interest of our company or our shareholders. In such cases, we may decide that the more prudent course of action is to simply monitor the situation or initiate or seek some other non-litigious action or solution.

Intellectual property disputes could cause us to spend substantial resources and distract our personnel from their normal responsibilities.

Litigation or other legal proceedings relating to intellectual property claims, with or without merit, is unpredictable and generally expensive and time-consuming and, even if resolved in our favor, is likely to divert significant resources from our core business, including distracting our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the market price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to adequately conduct such litigation or proceedings. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Accordingly, despite our efforts, we may not be able to prevent third parties from infringing upon or misappropriating or from successfully challenging our intellectual property rights. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a material adverse effect on our ability to compete in the marketplace.

We may not be able to protect our intellectual property rights throughout the world.

Filing, prosecuting and defending patents on all of our product candidates throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States may be less extensive than those in the United States. Many companies have encountered significant problems in protecting and defending intellectual property rights in certain foreign jurisdictions. The requirements for patentability differ, in varying degrees, from country to country. The legal systems of some countries, particularly developing countries, do not favor the enforcement of patent and other intellectual property rights, especially those relating to life sciences. In addition, the laws of some foreign countries do not protect intellectual property rights, including trade secrets, to the same extent as federal and state laws of the United States. This could make it difficult for us to stop the infringement of any patents we obtain or the misappropriation of our other intellectual property rights. In addition, many countries limit the enforceability of patents against third parties, including government agencies or government contractors. In these countries, patents may provide limited or no benefit. Moreover, our ability to protect and enforce our intellectual property rights may be adversely affected by unforeseen changes in foreign intellectual property laws.

Proceedings to enforce our patent rights in foreign jurisdictions, regardless of whether successful, would result in substantial costs and divert our efforts and attention from other aspects of our business. Furthermore, while we intend to protect our intellectual property rights in our expected significant markets, we cannot ensure that we will be able to initiate or maintain similar efforts in all jurisdictions in which we may wish to market our product candidates. Accordingly, our efforts to protect our intellectual property rights in such countries may be inadequate, which may have an adverse effect on our ability to successfully commercialize our product candidates in all of our expected significant foreign markets.

Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection but enforcement is not as strong as in the United States. These products may compete with our products in jurisdictions where we do not have any issued patents and our patent claims or other intellectual property rights may not be effective or sufficient to prevent them from so competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, particularly those relating to biopharmaceuticals, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial cost and divert our efforts and attention from other aspects of our business.

Similarly, if our trade secrets are disclosed in a foreign jurisdiction, competitors worldwide could have access to our proprietary information and we may be without satisfactory recourse. Such disclosure could have a material adverse effect on our business.

Obtaining and maintaining patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

The PTO and various non-US governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents and/or applications will be due to be paid to the PTO and various governmental patent agencies outside of the United States in several stages over the lifetime of the patents and/or applications. We employ reputable law firms and other professionals and rely on such third parties to help us comply with these requirements and effect payment of these fees with respect to the patent and patent applications that we own, and if we in-license intellectual property we may have to rely upon our licensors to comply with these requirements and effect payment of these fees with respect to any patents and patent applications that we license. In many cases, an inadvertent lapse can be cured by payment of a late fee or by other means in accordance with the applicable rules. However, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, our competitors might be able to enter the market and this circumstance would have a material adverse effect on our business.

Recent patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.

On September 16, 2011, the Leahy-Smith America Invents Act (Leahy-Smith Act) was signed into law. The Leahy-Smith Act includes a number of significant changes to United States patent law. These include provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. The PTO is currently developing regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first to file provisions, did not become effective until March 2013, 18 months after its enactment. Accordingly, it is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

Recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. Depending on decisions by the U.S.

Congress, the federal courts, and the PTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patent and patents that we might obtain in the future.

Intellectual property rights do not necessarily address all potential threats to our competitive advantage.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business or permit us to maintain our competitive advantage. The following examples are illustrative:

- others may be able to make compounds that are similar to our product candidates but that are not covered by the claims of our issued patent or any pending patent application we may have;
- we might not have been the first to make the inventions covered by the issued patent or pending patent application that we own;
- we might not have been the first to file patent applications covering an invention;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- pending patent applications that we own or license may not lead to issued patents;
- the issued patent that we own or any issued patents that we license may not provide us with any competitive advantages, or may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop or in-license additional proprietary technologies that are patentable; and
- the patents of others may have an adverse effect on our business.

Should any of these events occur, they could significantly harm our business, results of operations and prospects.

We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties or that our employees have wrongfully used or disclosed alleged trade secrets of former or other employers.

Many of our employees and consultants, including our senior management and our scientific founders, have been employed or retained at universities or by other biotechnology or pharmaceutical companies, including potential competitors. Some of our employees and consultants, including each member of our senior management and each of our scientific founders, executed proprietary rights, non-disclosure and non-competition agreements in connection with such previous employment or retention. Although we try to ensure that our employees and consultants do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or these employees or consultants have used or disclosed intellectual property, including trade secrets or other proprietary information, of any such employee's or consultant's former or other employer. We are not aware of any threatened or pending claims related to these matters or concerning the agreements with our senior management or scientific founders, but in the future litigation may be necessary to defend against such claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management.

We may be subject to claims challenging the inventorship or ownership of our issued patent, any patents issued as a result of our pending or future patent applications and other intellectual property.

We may also be subject to claims that former employees, collaborators or other third parties have an ownership interest in our issued patent, any patents issued as a result of our pending or future applications or other intellectual property. For example, we work with third-party contractors in formulating and manufacturing our product candidates. While we believe we have all rights to any intellectual property related to our product candidates, a third party-contractor may claim they have ownership rights. We have had in the past, and we may also have in the future, ownership disputes arising, for example, from conflicting obligations of consultants or others who are involved in developing our product candidates and technologies. For example, some of our consultants are employees of the University of Queensland. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.

Because we expect to rely on third parties in the development and manufacture of our product candidates, we must, at times, share trade secrets with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, consulting agreements or other similar agreements with our advisors, employees, third-party contractors and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, including our trade secrets. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor's discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may have an adverse effect on our business and results of operations.

In addition, these agreements typically restrict the ability of our advisors, employees, third-party contractors and consultants to publish data potentially relating to our trade secrets, although our agreements may contain certain limited publication rights. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of our agreements with third parties, independent development or publication of information by any of our third-party collaborators. A competitor's discovery of our trade secrets would impair our competitive position and have an adverse impact on our business.

We have not yet registered trademarks for a commercial trade name for our product candidates and failure to secure such registrations could adversely affect our business.

We have not yet registered trademarks for a commercial trade name for our product candidates. During trademark registration proceedings, we may receive rejections. Although we would be given an opportunity to respond to those rejections, we may be unable to overcome such rejections. In addition, in the PTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings may be filed against our trademarks, and our trademarks may not survive such proceedings. Moreover, any name we propose to use with our product candidates in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. The FDA typically conducts a review of proposed product names, including an evaluation of potential for confusion with other product names. If the FDA

objects to any of our proposed proprietary product names, we may be required to expend significant additional resources in an effort to identify a suitable substitute name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA.

We may not be successful in obtaining or maintaining necessary rights to our product candidates through acquisitions and in-licenses.

We may find that our programs require the use of proprietary rights held by third parties or the growth of our business may depend in part on our ability to acquire, in-license or use these proprietary rights. We may be unable to acquire or in-license compositions, methods of use, processes or other third party intellectual property rights from third parties that we identify as necessary for our product candidates. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of more established companies are also pursuing strategies to license or acquire third-party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, financial resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment. Even if we are able to obtain a license to intellectual property of interest, we may not be able to secure exclusive rights, in which case others could use the same rights and compete with us.

If we are unable to successfully obtain rights to required third party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of that program and our business and financial condition could suffer.

Any collaboration arrangements that we may enter into in the future may not be successful, which could adversely affect our ability to develop and commercialize our product candidates.

We may seek collaboration arrangements with pharmaceutical or biotechnology companies for the development or commercialization of our product candidates depending on the merits of retaining commercialization rights for ourselves as compared to entering into collaboration arrangements. We will face, to the extent that we decide to enter into collaboration agreements, significant competition in seeking appropriate collaborators. Moreover, collaboration arrangements are complex and time-consuming to negotiate, document, implement and maintain. We may not be successful in our efforts to establish and implement collaborations or other alternative arrangements should we so chose to enter into such arrangements. The terms of any collaborations or other arrangements that we may establish may not be favorable to us.

Any future collaborations that we enter into may not be successful. The success of our collaboration arrangements will depend heavily on the efforts and activities of our collaborators. Collaborations are subject to numerous risks, which may include that:

- collaborators have significant discretion in determining the efforts and resources that they will apply to collaborations;
- collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in their strategic focus due to the acquisition of competitive products, availability of funding or other external factors, such as a business combination that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial, abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates;

- a collaborator with marketing, manufacturing and distribution rights to one or more products may not commit sufficient resources to or otherwise not perform satisfactorily in carrying out these activities;
- we could grant exclusive rights to our collaborators that would prevent us from collaborating with others;
- collaborators may not properly maintain or defend our intellectual property rights or may use our intellectual property or proprietary information in a way that gives rise to actual or threatened litigation that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential liability;
- disputes may arise between us and a collaborator that causes the delay or termination of the research, development or commercialization of our current or future products or that results in costly litigation or arbitration that diverts management attention and resources;
- collaborations may be terminated, and, if terminated, may result in a need for additional capital to pursue further development or commercialization of the applicable current or future products;
- collaborators may own or co-own intellectual property covering our products that results from our collaborating with them, and in such cases, we would not have the exclusive right to develop or commercialize such intellectual property; and
- a collaborator's sales and marketing activities or other operations may not be in compliance with applicable laws resulting in civil or criminal proceedings.

Risks Related to This Offering and Ownership of our Common Stock

We do not know whether an active, liquid and orderly trading market will develop for our common stock or what the market price of our common stock will be and as a result it may be difficult for you to sell your shares of our common stock.

Prior to this offering there has been no market for shares of our common stock. Although we anticipate our common stock will be approved for listing on The NASDAQ Global Market, an active trading market for our shares may never develop or be sustained following this offering. The initial public offering price for our common stock was determined through negotiations with the underwriters, and the negotiated price may not be indicative of the market price of our common stock after this offering. This initial public offering price may vary from the market price of our common stock after the offering. Further, certain of our existing stockholders and their affiliated entities, including investors affiliated with certain of our directors, have indicated an interest in purchasing up to approximately $40.0 million in this offering and, to the extent these existing stockholders and their affiliated investors purchase shares in this offering, fewer shares may be actively traded in the public market because these stockholders will be restricted from selling the shares by restrictions under applicable securities laws, which would reduce the liquidity of the market for our common stock. The lack of an active market may impair your ability to sell your shares at the time you wish to sell them or at a price that you consider reasonable. In addition, as described further in these "Risk Factors," a substantial percentage of our common stock will continue to be held by our executive officers and existing investors (including any shares purchased in this offering), who will be subject to lock-up agreements expiring 180 days from the date of this prospectus (except that the lock-up will not apply to any shares purchased in this offering and will include other exemptions). As a result of these and other factors, you may be unable to resell your shares of our common stock at or above the initial public offering price. Further, an inactive market may also impair our ability to raise capital by selling shares of our common stock and may impair our ability to enter into strategic collaborations or acquire companies or products by using our shares of common stock as consideration.

The price of our stock may be volatile, and you could lose all or part of your investment.

The trading price of our common stock following this offering is likely to be highly volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. In addition to the factors discussed in these "Risk Factors" and elsewhere in this prospectus, these factors include, but are not limited to:

- any delay in the commencement, enrollment and ultimate completion of clinical trials;
- actual or anticipated results in our clinical trials or those of our competitors;
- positive outcomes, or faster development results than expected, by parties developing peptide-based product candidates that are competitive with our peptide-based product candidates, as well as approval of any such competitive peptide-based product candidates;
- failure to successfully develop commercial-scale manufacturing capabilities;
- unanticipated serious safety concerns related to the use of any of our peptide-based product candidates;
- failure to secure collaboration agreements for our peptide-based product candidates or actual or perceived unfavorable terms of such agreements;
- adverse regulatory decisions;
- changes in the structure of healthcare payment systems;
- changes in laws or regulations applicable to our product candidates, including but not limited to clinical trial requirements for approvals;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our peptide-based product candidates;
- our dependence on third parties, including CROs as well as manufacturers;
- our failure to successfully commercialize any of our peptide-based product candidates, if approved;
- additions or departures of key scientific or management personnel;
- failure to meet or exceed any financial guidance or development timelines that we may provide to the public;
- actual or anticipated variations in quarterly operating results;
- failure to meet or exceed the estimates and projections of the investment community;
- overall performance of the equity markets and other factors that may be unrelated to our operating performance or the operating performance of our competitors, including changes in market valuations of similar companies;
- conditions or trends in the biotechnology and biopharmaceutical industries;
- announcements of significant acquisitions, strategic collaborations, joint ventures or capital commitments by us or our competitors;
- our ability to maintain an adequate rate of growth and manage such growth;
- issuances of debt or equity securities;
- significant lawsuits, including patent or stockholder litigation;
- sales of our common stock by us or our stockholders in the future;
- trading volume of our common stock;

- publication of research reports about us or our industry or positive or negative recommendations or withdrawal of research coverage by securities analysts;
- ineffectiveness of our internal controls;
- general political and economic conditions; and
- effects of natural or man-made catastrophic events.

In addition, the stock market in general, and The NASDAQ Global Market and biotechnology companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance. The realization of any of the above risks or any of a broad range of other risks, including those described in these "Risk Factors," could have a dramatic and material adverse impact on the market price of our common stock.

We have broad discretion in the use of the net proceeds from this offering and may not use them effectively.

Our management will have broad discretion in the application of the net proceeds from this offering. You will not have the opportunity, as part of your investment decision, to assess whether the proceeds are being used appropriately. Further, our management might not apply our net proceeds in ways that ultimately increase the value of your investment. If we do not invest or apply the net proceeds from this offering in ways that enhance stockholder value, we may fail to achieve expected financial results, which could cause our stock price to decline.

Volatility in our share price could subject us to securities class action litigation.

Securities class action litigations have often been brought against companies following a decline in the market price of their securities. This risk is especially relevant for us because pharmaceutical companies have experienced significant share price volatility in recent years. If we face such litigation, it could result in substantial costs and a diversion of management's attention and resources, which could harm our business.

Our principal stockholders and management own a significant percentage of our stock after this offering and will be able to exert significant control over matters subject to stockholder approval.

As of June 30, 2016, our executive officers, directors, holders of 5% or more of our capital stock and their respective affiliates beneficially owned approximately 93.4% of our stock and, upon the closing of this offering, assuming the purchase of $40.0 million of shares of our common stock by entities affiliated with certain of our existing stockholders and directors who have indicated an interest in purchasing such shares in this offering (or 3,333,333 shares at an assumed initial public offering price of $12.00 per share, the midpoint of the price range set forth on the cover page of this prospectus) that same group will hold approximately 79.1% of our outstanding stock. Therefore, even after this offering these stockholders will have substantial influence and may be able to determine all matters requiring stockholder approval. For example, these stockholders may be able to control elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This concentration of voting power could, among other things, delay or prevent an acquisition of our company on terms that other stockholders may desire, which in turn could depress our stock price and may prevent attempts by our stockholders to replace or remove the board of directors or management.

We have identified a material weakness in our internal control over financial reporting and may identify additional material weaknesses in the future or otherwise fail to maintain an effective system of internal controls, which may result in material misstatements of our financial statements or cause us to fail to meet our periodic reporting obligations.

Prior to this offering, we were a private company and had limited accounting and financial reporting personnel and other resources with which to address our internal controls and procedures. In connection with the audit of our consolidated financial statements for the years ended December 31, 2014 and 2015, we and our independent registered public accounting firm identified two material weaknesses in our internal control over financial reporting. A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting such that there is a reasonable possibility that a material misstatement of our annual or interim financial statements will not be prevented or detected on a timely basis.

The first material weakness related to a deficiency in the operation of our internal controls over the accounting for non-routine, complex equity transactions, which resulted in material post-closing adjustments to the convertible preferred stock, additional paid-in capital, interest expense, and gain from modification of the redeemable convertible preferred stock balances in the consolidated financial statements for the year ended December 31, 2013. Our lack of adequate accounting personnel has resulted in the identification of a second material weakness in our internal control over financial reporting for the years ended December 31, 2014 and 2015. Specifically, we did not, and have not historically, appropriately designed and implemented controls over the review and approval of manual journal entries and the related supporting journal entry calculations.

Neither we nor our independent registered public accounting firm has performed or was required to perform an evaluation of our internal control over financial reporting in according with Section 404 of the Sarbanes-Oxley Act. We intend to take steps to remediate the material weaknesses, including increasing the depth and experience within our accounting and finance organization, as well as designing and implementing improved processes and internal controls. While we intend to implement a plan to remediate the material weaknesses, we are in the early phases of the implementation of this plan and we will not complete our implementation until after this offering is completed. We cannot predict the success of such plan or the outcome of our assessment of these plans at this time. We can give no assurance that this implementation will remediate this deficiency in internal control or that additional material weaknesses or significant deficiencies in our internal control over financial reporting will not be identified in the future. Our failure to implement and maintain effective internal control over financial reporting could result in errors in our financial statements that could result in a restatement of our financial statements, cause us to fail to meet our reporting obligations.

As a result of becoming a public company, we will be obligated to develop and maintain proper and effective internal controls over financial reporting and any failure to maintain the adequacy of these internal controls may adversely affect investor confidence in our company and, as a result, the value of our ordinary shares.

We will be required, pursuant to Section 404 of the Sarbanes-Oxley Act (Section 404), to furnish a report by management on the effectiveness of our internal control over financial reporting for the first fiscal year beginning after the effective date of this offering. This assessment will need to include disclosure of any material weaknesses identified by our management in our internal control over financial reporting. Our independent registered public accounting firm will not be required to attest to the effectiveness of our internal control over financial reporting until our first annual report required to be filed with the SEC following the date we are no longer an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012 (the JOBS Act). At such time as we are required to obtain auditor attestation, if we then have a material weakness, we would receive an adverse opinion regarding our internal control over financial reporting from our independent registered accounting firm.

We are beginning the costly and challenging process of compiling the system and processing documentation necessary to perform the evaluation needed to comply with Section 404, and we may not be able to complete our evaluation, testing and any required remediation in a timely fashion. Our compliance with Section 404 will

require that we incur substantial accounting expense and expend significant management efforts. We currently do not have an internal audit group, and we will need to hire additional accounting and financial staff with appropriate public company experience and technical accounting knowledge and compile the system and process documentation necessary to perform the evaluation needed to comply with Section 404.

During our evaluation of our internal control, if we identify one or more material weaknesses in our internal control over financial reporting or fail to remediate our current material weaknesses, we will be unable to assert that our internal control over financial reporting is effective. We cannot assure you that there will not be material weaknesses or significant deficiencies in our internal control over financial reporting in the future. Any failure to maintain internal control over financial reporting could severely inhibit our ability to accurately report our financial condition or results of operations. If we are unable to conclude that our internal control over financial reporting is effective, or if our independent registered public accounting firm determines we have a material weakness or significant deficiency in our internal control over financial reporting, we could lose investor confidence in the accuracy and completeness of our financial reports, the market price of our ordinary shares could decline, and we could be subject to sanctions or investigations by NASDAQ, the SEC or other regulatory authorities. Failure to remedy any material weakness in our internal control over financial reporting, or to implement or maintain other effective control systems required of public companies, could also restrict our future access to the capital markets.

We are an "emerging growth company" and as a result of the reduced disclosure and governance requirements applicable to emerging growth companies, our common stock may be less attractive to investors.

We are an "emerging growth company" as defined in the JOBS Act, and we intend to take advantage of some of the exemptions from reporting requirements that are applicable to other public companies that are not emerging growth companies, including:

- being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure;
- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation; and
- not being required to hold a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

We will remain an emerging growth company, and thus may continue to rely on these exemptions, until the earlier of (1) the last day of the fiscal year (a) following the fifth anniversary of the completion of this offering, (b) in which we have total annual gross revenue of at least $1.0 billion, or (c) in which we are deemed to be a large accelerated filer, which means the market value of our common stock that is held by non-affiliates exceeds $700 million as of the prior June 30th, and (2) the date on which we have issued more than $1.0 billion in non-convertible debt during the prior three-year period.

Under Section 107(b) of the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have irrevocably elected not to avail ourselves of this exemption, and, therefore, we will be subject to the same new or revised accounting standards as other public companies that are not "emerging growth companies."

If you purchase our common stock in this offering, you will incur immediate and substantial dilution in the book value of your stock.

The initial public offering price of our common stock will be substantially higher than the as adjusted net tangible book value per common share of our common stock. Therefore, if you purchase our common stock in this offering, you will pay a price per common share that substantially exceeds the book value of our tangible assets after subtracting our liabilities. Based on an assumed initial public offering price of $12.00 per common share, which is the midpoint of the price range set forth on the cover page of this prospectus, you will experience immediate dilution of $5.91 per common share, representing the difference between our as adjusted net tangible book value per common share as of March 31, 2016, after giving effect to this offering, and the assumed initial public offering price. Further, the future exercise of any outstanding options to purchase our common stock will cause you to experience additional dilution. See the section titled "Dilution" for additional information.

Future sales of our common stock may depress our share price.

Sales of a substantial number of shares of our common stock in the public market after this offering, or the perception that these sales might occur, could depress the market price of our common stock and could impair our ability to raise capital through the sale of additional equity securities. Of our issued and outstanding common stock, all of the shares sold in this offering will be freely transferable without restrictions or further registration under the Securities Act of 1933, as amended (the Securities Act), except for any stock acquired by our affiliates, as defined in Rule 144 under the Securities Act. Substantially all of the remaining shares outstanding after this offering will be restricted as a result of lock-up agreements for 180 days after the date of this prospectus. See the section titled "Underwriting—No Sales of Similar Securities" for a more detailed description of the lock-up period. In addition, as of March 31, 2016, 783,341 million shares of common stock that are subject to outstanding options, will become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules, the Lock-up Agreements and Rule 144 and Rule 701 under the Securities Act. If these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

We intend to file a registration statement on Form S-8 under the Securities Act to register the total number of our common stock that may be issued under our equity incentive plans. This registration statement will become effective immediately upon filing, and shares covered by this registration statement will be eligible for sale in the public markets, subject to Rule 144 limitations applicable to affiliates, the terms of the applicable plan and the option agreements entered into with option holders, and any lock-up agreements described above. Sales of this stock have an adverse effect on the trading price of our common stock. In addition, in the future we may issue common stock or other securities if we need to raise additional capital. The number of our new common stock issued in connection with raising additional capital could constitute a material portion of our then outstanding common stock.

If we sell shares of our common stock in future financings, stockholders may experience immediate dilution and, as a result, our stock price may decline.

We may from time to time issue additional shares of common stock at a discount from the current trading price of our common stock. As a result, our stockholders would experience immediate dilution upon the purchase of any shares of our common stock sold at such discount. In addition, as opportunities present themselves, we may enter into financing or similar arrangements in the future, including the issuance of debt securities, preferred stock or common stock. If we issue common stock or securities convertible into common stock, our common stockholders would experience additional dilution and, as a result, our stock price may decline.

We will incur increased costs as a result of operating as a public company, and our management will be required to devote substantial time to compliance with our public company responsibilities and corporate governance practices.

We will incur significant legal, accounting and other expenses as a public company, including costs resulting from public company reporting obligations under the Securities Exchange Act of 1934, as amended (the Exchange Act), and regulations regarding corporate governance practices. The listing requirements of The NASDAQ Global Market require that we satisfy certain corporate governance requirements relating to director independence, distributing annual and interim reports, stockholder meetings, approvals and voting, soliciting proxies, conflicts of interest and a code of conduct. Our management and other personnel will need to devote a substantial amount of time to ensure that we comply with all of these requirements, and we will likely need to hire additional accounting and financial staff with appropriate public company reporting experience and technical accounting knowledge. Moreover, the reporting requirements, rules and regulations will increase our legal and financial compliance costs and will make some activities more time consuming and costly. Any changes we make to comply with these obligations may not be sufficient to allow us to satisfy our obligations as a public company on a timely basis, or at all. These reporting requirements, rules and regulations, coupled with the increase in potential litigation exposure associated with being a public company, could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors or board committees or to serve as executive officers, or to obtain certain types of insurance, including directors' and officers' insurance, on acceptable terms.

As a public company, and particularly after we are no longer an "emerging growth company," we will incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The NASDAQ Global Market and other applicable securities rules and regulations impose various requirements on public companies. Our management and other personnel will need to devote a substantial amount of time to compliance with these requirements. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect that these rules and regulations may make it more difficult and more expensive for us to obtain directors' and officers' liability insurance, which could make it more difficult for us to attract and retain qualified members of our board of directors. We cannot predict or estimate the amount of additional costs we will incur as a public company or the timing of such costs.

Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

Upon completion of this offering, we will become subject to the periodic reporting requirements of the Exchange Act. Our disclosure controls and procedures are designed to reasonably assure that information required to be disclosed by us in reports we file or submit under the Exchange Act is accumulated and communicated to management, recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met.

These inherent limitations include the realities that judgments in decision- making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements due to error or fraud may occur and not be detected.

To date, we have never conducted a review of our internal control for the purpose of providing the reports required by these rules. During the course of our review and testing, we may identify deficiencies and be unable to remediate them before we must provide the required reports. Furthermore, if we have a material weakness in our internal controls over financial reporting, we may not detect errors on a timely basis and our financial

statements may be materially misstated. We or our independent registered public accounting firm may not be able to conclude on an ongoing basis that we have effective internal control over financial reporting, which could harm our operating results, cause investors to lose confidence in our reported financial information and cause the trading price of our stock to fall. In addition, as a public company we will be required to file accurate and timely quarterly and annual reports with the SEC under the Exchange Act. Any failure to report our financial results on an accurate and timely basis could result in sanctions, lawsuits, delisting of our shares from The NASDAQ Global Market or other adverse consequences that would materially harm our business.

NASDAQ may delist our securities from its exchange, which could limit investors' ability to make transactions in our securities and subject us to additional trading restrictions.

We have applied to list our common stock on The NASDAQ Global Market. In order to make a final determination of compliance with their listing criteria, NASDAQ may look to the first trading day's activity and, particularly, the last bid price on such day. In the event the trading price for our common stock drops below The NASDAQ Global Market's $1.00 minimum bid requirement, NASDAQ could rescind our initial listing approval. If that were to happen, the liquidity for our common stock would decrease, which may substantially decrease the trading price of our common stock.

In addition, we cannot assure you that, in the future, our securities will meet the continued listing requirements to be listed on The NASDAQ Global Market. If The NASDAQ Global Market delists our common stock, we could face significant material adverse consequences, including:

- a limited availability of market quotations for our securities;
- a determination that our common stock is a "penny stock" which will require brokers trading in our common stock to adhere to more stringent rules and possibly resulting in a reduced level of trading activity in the secondary trading market for our common stock;
- a limited amount of news and analyst coverage for our company; and
- a decreased ability to issue additional securities or obtain additional financing in the future.

If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, our stock price and trading volume could decline.

The trading market for our common stock will be influenced the research and reports that securities or industry analysts publish about us or our business. Securities and industry analysts do not currently, and may never, publish research on our company. If no securities or industry analysts commence coverage of our company, the trading price for our stock would likely be negatively impacted. In the event securities or industry analysts initiate coverage, if one or more of the analysts who cover us downgrade our stock or publish inaccurate or unfavorable research about our business, our stock price could be adversely affected. If one or more of these analysts cease coverage of our company or fail to publish reports on us regularly, demand for our common stock could decrease, and we could lose visibility in the financial markets, which might cause our stock price and trading volume to decline.

Claims for indemnification by our directors and officers may reduce our available funds to satisfy successful third party claims against us and may reduce the amount of money available to us generally.

Our amended and restated certificate of incorporation provides that we will indemnify our directors and officers, in each case to the fullest extent permitted by Delaware law.

In addition, as permitted by Section 145 of the Delaware General Corporation Law, our amended and restated bylaws to be effective immediately prior to the completion of this offering and our indemnification agreements that we have entered into and will enter into with our directors and officers provide that:

- we will indemnify our directors and officers for serving us in those capacities or for serving other business enterprises at our request, to the fullest extent permitted by Delaware law. Delaware law provides that a corporation may indemnify such person if such person acted in good faith and in a manner such person reasonably believed to be in or not opposed to the best interests of the registrant and, with respect to any criminal proceeding, had no reasonable cause to believe such person's conduct was unlawful;
- we may, in our discretion, indemnify employees and agents in those circumstances where indemnification is permitted by applicable law;
- we are required to advance expenses, as incurred, to our directors and officers in connection with defending a proceeding, except that such directors or officers shall undertake to repay such advances if it is ultimately determined that such person is not entitled to indemnification;
- we will not be obligated pursuant to our bylaws to indemnify a person with respect to proceedings initiated by that person against us or our other indemnitees, except with respect to proceedings authorized by our board of directors or brought to enforce a right to indemnification;
- the rights conferred in our bylaws are not exclusive, and we are authorized to enter into indemnification agreements with our directors, officers, employees and agents and to obtain insurance to indemnify such persons; and
- we may not retroactively amend our bylaw provisions to reduce our indemnification obligations to directors, officers, employees and agents.

As a result, if we are required to indemnify one or more of our directors or executive officers, it may reduce our available funds to satisfy successful third party claims against us, may reduce the amount of money available to us and may have a material adverse effect on our business and financial condition.

Because we do not anticipate paying any cash dividends on our common stock in the foreseeable future, capital appreciation, if any, would be your sole source of gain.

We have never declared or paid any cash dividends on our common stock. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. As a result, capital appreciation, if any, of our common stock would be your sole source of gain on an investment in our common stock for the foreseeable future. See "Dividend Policy" for additional information.

Provisions in our corporate charter documents could make an acquisition of us more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our certificate of incorporation and our bylaws may discourage, delay or prevent a merger, acquisition or other change in control of us that stockholders may consider favorable, including transactions in which stockholders might otherwise receive a premium for their shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Because our board of directors is responsible for appointing the members of our management team, these provisions could in turn affect any attempt by our stockholders to replace current members of our management team. Among others, these provisions include the following:

Our amended and restated certificate of incorporation will provide that the Court of Chancery of the State of Delaware will be the exclusive forum for substantially all disputes between us and our stockholders, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers or employees.

Our amended and restated certificate of incorporation, as we expect it to be in effect upon the closing of this offering, will provide that the Court of Chancery of the State of Delaware will be the exclusive forum for any derivative action or proceeding brought on our behalf; any action asserting a breach of fiduciary duty; any action asserting a claim against us arising pursuant to the Delaware General Corporation Law, our amended and restated certificate of incorporation or our bylaws; or any action asserting a claim against us that is governed by the internal affairs doctrine. The choice of forum provision may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers or other employees, which may discourage such lawsuits against us and our directors, officers and other employees. Alternatively, if a court were to find the choice of forum provision contained in our amended and restated certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could adversely affect our business and financial condition.

Our board of directors has certain characteristics which may delay or prevent a change of our management or a change in control.

Our board of directors has the following characteristics which may delay or prevent a change of management or a change in control:

- our board of directors has the right to elect directors to fill a vacancy created by the expansion of the board of directors or the resignation, death or removal of a director, which prevents stockholders from being able to fill vacancies on our board of directors;
- our stockholders may not act by written consent or call special stockholders' meetings; as a result, a holder, or holders, controlling a majority of our capital stock would not be able to take certain actions other than at annual stockholders' meetings or special stockholders' meetings called by the board of directors, the chairman of the board or the chief executive officer;
- our certificate of incorporation does not provide for cumulative voting in the election of directors, which limits the ability of minority stockholders to elect director candidates;
- stockholders must provide advance notice and additional disclosures in order to nominate individuals for election to the board of directors or to propose matters that can be acted upon at a stockholders' meeting, which may discourage or deter a potential acquiror from conducting a solicitation of proxies to elect the acquiror's own slate of directors or otherwise attempting to obtain control of our company; and
- our board of directors may issue, without stockholder approval, shares of undesignated preferred stock; the ability to issue undesignated preferred stock makes it possible for our board of directors to issue preferred stock with voting or other rights or preferences that could impede the success of any attempt to acquire us.

Our ability to utilize our net operating loss carryforwards and certain other tax attributes may be limited.

We have incurred substantial losses during our history. We do not anticipate generating revenue from sales of products for the foreseeable future, if ever, and we may never achieve profitability. To the extent that we continue to generate taxable losses, unused losses will carry forward to offset future taxable income, if any, until such unused losses expire. Under Section 382 of the Internal Revenue Code of 1986, as amended (the Code), if a corporation undergoes an "ownership change" (generally defined as a greater than 50 percentage points change (by value) in its equity ownership over a rolling three-year period), the corporation's ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes to offset its post-change income may be limited. We have not completed our analysis to determine what, if any, impact any prior ownership change has

had on our ability to utilize our net operating loss carryforwards. In addition, we may experience ownership changes in the future as a result of this offering or subsequent shifts in our stock ownership, some of which are outside our control. As of December 31, 2015, we had federal net operating loss carryforwards of approximately $20.0 million that could be limited if we have experienced, or if in the future we experience, an ownership change, which could have an adverse effect on our future results of operations.

Provisions under Delaware law and California law could make an acquisition of our company more difficult, limit attempts by our stockholders to replace or remove our current management and limit the market price of our common stock.

Because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which generally prohibits a Delaware corporation from engaging in any of a broad range of business combinations with any holder of at least 15% of our capital stock for a period of three years following the date on which the stockholder acquired at least 15% of our common stock. Likewise, because our principal executive offices are located in California, the anti-takeover provisions of the California Corporations Code may apply to us under certain circumstances now or in the future. See the section of this prospectus titled “Delaware Anti-Takeover Statute” for additional information.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains forward-looking statements. All statements other than statements of historical facts contained in this prospectus, including statements regarding our future results of operations and financial position, business strategy, current and future product offerings, reimbursement and coverage, research and development costs, timing and likelihood of success and plans and objectives of management for future operations are forward-looking statements. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements.

In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "expect," "plan," "anticipate," "could," "intend," "target," "project," "contemplates," "believes," "estimates," "predicts," "potential" or "continue" or the negative of these terms or other similar expressions. The forward-looking statements in this prospectus are only predictions.

A number of important factors could cause our actual results to differ materially from those indicated in these forward-looking statements, including those factors identified in "Risk Factors" or "Management's Discussion and Analysis of Financial Condition and Results of Operations" or the following:

- the initiation, cost, timing, progress and results of our research and development activities, including pre-clinical and clinical studies;
- our ability to obtain and maintain regulatory approval for our product candidates;
- our ability to obtain funding for our operations;
- our plans to research, develop and commercialize our product candidates;
- our ability to obtain and maintain intellectual property protection for our product candidates;
- the size and growth potential of the markets for our product candidates, and our ability to serve those markets;
- our ability to successfully commercialize our product candidates, if approved;
- the rate and degree of market acceptance of our product candidates, if approved;
- our ability to develop sales and marketing capabilities, whether alone or with potential collaborators, to commercialize our product candidates, if approved;
- regulatory developments in the United States and foreign countries;
- the performance of third parties in connection with the development of our product candidates, including third parties conducting our clinical trials as well as third-party suppliers and manufacturers;
- the development, regulatory approval and commercial success of competing therapies;
- our ability to attract and retain key scientific or management personnel;
- our expectations regarding the time during which we will be an emerging growth company under the JOBS Act;
- our use of the net proceeds from this offering; and
- the accuracy of our estimates regarding expenses, future revenues, capital requirements and need for additional financing.

We have based these forward-looking statements largely on our current expectations and projections about future events and financial trends that we believe may affect our business, financial condition and results of operations. These forward-looking statements speak only as of the date of this prospectus and are subject to a number of risks, uncertainties and assumptions described under the sections in this prospectus entitled "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" and elsewhere in this prospectus. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond our control, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. Moreover, we operate in an evolving environment.

New risk factors and uncertainties may emerge from time to time, and it is not possible for management to predict all risk factors and uncertainties. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise. The forward-looking statements contained in this prospectus are excluded from the safe harbor protection provided by the Private Securities Litigation Reform Act of 1995 and Section 27A of the Securities Act of 1933, as amended.

This prospectus also contains estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

MARKET AND INDUSTRY DATA

This prospectus also contains estimates, projections and other information concerning our industry, the market in which we operate and our business. Unless otherwise indicated, information contained in this prospectus concerning our industry and the market in which we operate, including our general expectations and market position, market opportunity and market size, is based on information from various sources, such as reports, research surveys, studies and similar data prepared by third parties, industry, medical and general publications, government data and similar sources and is subject to a number of assumptions and limitations. Although we are responsible for all of the disclosure contained in this prospectus and we believe the information from the third-party sources included in this prospectus is reliable, such information is inherently imprecise. The industry in which we operate is subject to a high degree of uncertainty and risk due to a variety of factors, including those described in the section titled "Risk Factors." These and other factors could cause results to differ materially from those expressed in the estimates made by the independent parties and by us. In some cases, we do not expressly refer to the sources from which these data are derived. In that regard, when we refer to one or more sources of this type of data in any paragraph, you should assume that other data of this type appearing in the same paragraph are derived from the same sources, unless otherwise expressly stated or the context otherwise requires.

USE OF PROCEEDS

We estimate that the net proceeds to us from the sale of 5,835,000 shares of common stock in this offering will be approximately $62.0 million (or approximately $71.8 million if the underwriters exercise their option to purchase additional shares in full), assuming an initial public offering price of $12.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

Each $1.00 increase (decrease) in the assumed initial public offering price of $12.00 per share would increase (decrease) the net proceeds to us from this offering by approximately $5.4 million, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions and estimated offering expenses payable by us. We may also increase or decrease the number of shares we are offering. Each increase (decrease) of 1,000,000 in the number of shares we are offering would increase (decrease) the net proceeds to us from this offering, after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us, by approximately $11.2 million, assuming the assumed initial public offering price stays the same.

The principal purposes of this offering are to obtain additional capital to support our operations, to create a public market for our common stock and to facilitate our future access to the public equity markets. We intend to use the net proceeds from this offering as follows:

- approximately $33.0 million to fund continued development of PTG-100 through the completion of a Phase 2b clinical trial;
- approximately $6.0 million to advance PTG-200 to complete IND-enabling studies and to begin a Phase 1 clinical trial;
- approximately $5.0 million to complete IND-enabling studies for PTG-300;
- approximately $2.0 million to fund our research and discovery activities related to additional product candidates; and
- the remaining proceeds for working capital and other general corporate purposes.

We believe, based on our current operating plan and expected expenditures that the net proceeds from this offering and our existing cash, cash equivalents, and available-for-sale securities will be sufficient to fund our operations for at least the next 18 months.

The amounts and timing of our actual expenditures will depend on numerous factors, including the results of our research and development effort, the timing and success of our ongoing pre-clinical studies and clinical trials, and pre-clinical studies and clinical trials we may begin in the future, the timing of our regulatory submissions, the factors described under “Risk Factors” in this prospectus, and the amount of cash used in our operations. We therefore cannot predict with certainty the amount of net proceeds from this offering to be used for the purposes described above.

In addition, in the event we identify other opportunities that we believe are in the best interests of our stockholders, we may also use a portion of the net proceeds to in-license, acquire or invest in complementary businesses, medicines, technologies or products, although we have no current commitments or obligations to do so. The costs and timing of the expansion of our sales and marketing capabilities and the conduct of our research and development activities are highly uncertain, subject to substantial risks and can often change. Depending on the outcome of these activities, our plans and priorities may change, and we may apply the net proceeds from this offering differently than we currently anticipate. As a result, we will have broad discretion in the application of the net proceeds.

Pending the uses described above, we plan to invest the net proceeds from this offering in short- and intermediate-term, interest-bearing obligations, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the U.S. government.

DIVIDEND POLICY

We have never declared or paid any cash dividends on our capital stock. We intend to retain future earnings, if any, to finance the operation of our business and do not anticipate paying any cash dividends in the foreseeable future. Any future determination related to dividend policy will be made at the discretion of our board of directors after considering our financial condition, results of operations, capital requirements, business prospects and other factors the board of directors deems relevant, and subject to the restrictions contained in any future financing instruments.

CAPITALIZATION

The following table sets forth our cash, cash equivalents and available-for-sale securities and capitalization as of March 31, 2016:

- on an actual basis;
- on a pro forma basis to reflect (i) the conversion of all of outstanding shares of our redeemable convertible preferred stock into an aggregate of 8,439,641 shares of common stock; and (ii) the reclassification of the redeemable convertible preferred stock warrant liability to consolidated stockholders' equity immediately prior to the closing of this offering as the warrants to purchase redeemable convertible preferred stock will be exercised, converted into warrants to purchase common stock or expired unexercised on May 10, 2016; and
- on a pro forma as adjusted basis to give further effect to the receipt of $62.0 million in net proceeds from our sale of shares of common stock in this offering at an assumed initial public offering price of $12.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, after deducting the estimated underwriting discount and commissions and estimated offering expenses payable by us.

The information in this table is illustrative only and our capitalization following the completion of this offering will be adjusted based on the actual initial public offering price and other terms of this offering determined at pricing. You should read this information together with our consolidated financial statements and related notes appearing elsewhere in this prospectus and the information set forth under the heading "Selected Consolidated Financial Data" and "Management's Discussion and Analysis of Financial Condition and Results of Operations."

	As of March 31, 2016		
	Actual	Pro Forma	Pro Forma As Adjusted(1)
	(Unaudited) (In thousands, except per share data)		
Cash, cash equivalents and available-for-sale securities	$ 29,022	$ 29,002	$ 91,041
Redeemable convertible preferred stock warrant liability	$ 1,005	$ —	$ —
Redeemable convertible preferred stock, $0.00001 par value per share — 126,374,911 shares authorized; 122,374,911 shares issued and outstanding, actual; no shares issued and outstanding, pro forma and pro forma as adjusted	65,361	—	—
Stockholders' (deficit) equity:			
Preferred stock, par value of $0.00001 per share, no shares authorized, issued or outstanding, actual; 10,000,000 shares authorized, no shares issued or outstanding, pro forma and pro forma as adjusted	—	—	—
Common stock, $0.00001 par value per share — 160,000,000 shares authorized; 383,910 shares issued and outstanding as of March 31, 2016, actual; 90,000,000 shares authorized, 8,823,551 shares issued and outstanding, pro forma and 14,658,551 shares issued and outstanding, pro forma as adjusted	—	—	—
Additional paid-in capital	277	66,643	128,662
Accumulated other comprehensive loss	(95)	(95)	(95)
Accumulated deficit	(39,162)	(39,162)	(39,162)
Total stockholders' (deficit) equity	(38,980)	27,386	89,405
Total capitalization	$ 27,386	$ 27,386	$ 89,405

(1) Each $1.00 increase (decrease) in the assumed initial public offering price of $12.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease), the amount of cash, cash equivalents and available-for-sale securities, additional paid-in capital, total stockholder's equity and total capitalization by $5.4 million, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting the estimated underwriting discount and commissions and estimated offering expenses payable by us. We may also increase or decrease the number of shares we are offering. An increase (decrease) of 1,000,000 in the number of shares we are offering would increase (decrease) the amount of cash, cash equivalents and available-for-sale securities, additional paid-in capital, total stockholder's equity and total capitalization by approximately $11.2 million, assuming the assumed initial public offering price per share, as set forth on the cover page of this prospectus, remains the same. The pro forma as adjusted information is illustrative only, and we will adjust this information based on the actual initial public offering price and other terms of this offering determined at pricing.

The number of shares of common stock issued and outstanding presented in the table above excludes the following shares as of March 31, 2016:

- 783,341 shares of our common stock issuable upon exercise of stock options outstanding under our 2007 Stock Option and Incentive Plan (2007 Plan), as amended, at a weighted average exercise price of $1.32 per share;
- 582,582 shares of our common stock issuable upon the exercise of stock options granted after March 31, 2016 at a weighted-average exercise price of $4.39 per share;
- 1,999,998 shares of redeemable preferred stock (convertible into 137,930 shares of common stock) issued pursuant to the exercise of preferred stock warrants after March 31, 2016;
- 52,948 shares of common stock reserved for issuance pursuant to future awards under our 2007 Plan, which will become available for issuance under our 2016 Plan upon the completion of this offering;
- 1,200,000 shares of common stock reserved, subject to increase on an annual basis, reserved for future issuance pursuant to our 2016 Plan, which will become effective upon completion of this offering as well as any automatic increases in the number of shares of common stock reserved for future issuance under the 2016 Plan; and
- 150,000 shares of our common stock reserved for future issuance under the 2016 ESPP, which will become effective upon completion of this offering, as well as any automatic increases in the number of shares of common stock reserved for future issuance under the 2016 ESPP.

DILUTION

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

As of March 31, 2016, we had a historical net tangible book value (deficit) of $(39.1) million, or $(101.89) per share of common stock. Our historical net tangible book value (deficit) per share represents total tangible assets less total liabilities and redeemable convertible preferred stock, divided by the number of shares of common stock outstanding as of March 31, 2016.

As of March 31, 2016, our pro forma net tangible book value was $27.3 million, or $3.09 per share of common stock. Our pro forma net tangible book value per share represents the amount of our total tangible assets reduced by the amount of our total liabilities and divided by the total number of shares of our common stock outstanding as of March 31, 2016, assuming the conversion of all outstanding shares of our redeemable convertible preferred stock into 8,439,641 shares of our common stock, which conversion will occur upon the completion of the offering and the reclassification of warrants to purchase redeemable convertible preferred stock that will be exercised, converted into warrants to purchase common stock or expired unexercised on May 10, 2016, and the related reclassification of our redeemable convertible preferred stock warrant liability to stockholders' equity.

After giving further effect to the sale of 5,835,000 shares of common stock that we are offering at an assumed initial public offering price of $12.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, and after deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma as adjusted net tangible book value as of March 31, 2016 would have been approximately $89.3 million, or approximately $6.09 per share. This amount represents an immediate increase in pro forma net tangible book value of $3.00 per share to our existing stockholders and an immediate dilution in pro forma net tangible book value of approximately $5.91 per share to new investors purchasing shares of common stock in this offering.

Dilution per share to new investors is determined by subtracting pro forma as adjusted net tangible book value per share after this offering from the initial public offering price per share paid by new investors. The following table illustrates this dilution (without giving effect to any exercise by the underwriters of their option to purchase additional shares):

Assumed initial public offering price per share		$12.00
Historical net tangible book value (deficit) per share as of March 31, 2016	$(101.89)	
Pro forma increase in historical net tangible book value per share attributable to the pro forma transactions described in the preceding paragraphs	104.98	
Pro forma net tangible book value per share as of March 31, 2016	$ 3.09	
Increase in pro forma net tangible book value per share attributable to this offering	3.00	
Pro forma as adjusted net tangible book value per share after this offering		6.09
Dilution per share to new investors in this offering		$ 5.91

Each $1.00 increase (decrease) in the assumed initial public offering price of $12.00 per share, the midpoint of the price range set forth on the cover page of this prospectus, would increase (decrease) the pro forma as adjusted net tangible book value per share after this offering by approximately $0.37, and dilution in pro forma net tangible book value per share to new investors by approximately $0.63, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting the estimated underwriting discounts and commissions and the estimated offering expenses payable by us. Each increase (decrease) of 1,000,000 shares in the number of shares offered by us would increase (decrease) our pro forma as adjusted net tangible book value per share after this offering by approximately $0.32 and $(0.37) per

share and decrease (increase) the dilution to investors participating in this offering by approximately $(0.32) and $0.37 per share, assuming that the assumed initial public offering price remains the same, and after deducting the estimated underwriting discounts and commissions and the estimated offering expenses payable by us.

If the underwriters exercise their option to purchase 875,250 additional shares of our common stock in full in this offering, the pro forma as adjusted net tangible book value after the offering would be $6.38 per share, the increase in pro forma net tangible book value per share to existing stockholders would be $3.29 per share and the dilution per share to new investors would be $5.62 per share, in each case assuming an initial public offering price of $12.00 per share, the midpoint of the price range set forth on the cover page of this prospectus.

The following table summarizes, on the pro forma as adjusted basis described above, as of March 31, 2016, the differences between the number of shares purchased from us, the total consideration paid to us in cash and the average price per share paid by existing stockholders for shares issued prior to this offering and the price to be paid by new investors in this offering. The calculation below is based on the assumed initial public offering price of $12.00 per share, the midpoint of the price range set forth on the cover page of the prospectus, before deducting the estimated underwriting discounts and commissions and estimated offering expenses payable by us.

	Shares Purchased		Total Consideration		Average Price Per Share
	Number	Percent	Amount	Percent	
Existing stockholders[1]	8,823,551	60.2%	$ 67,436,000	49.1%	$ 7.64
New investors[1]	5,835,000	39.8	70,020,000	50.9	12.00
Total	14,658,551	100%	137,456,000	100%	9.38

(1) Certain of our existing stockholders and their affiliated entities, including investors affiliated with certain of our directors, have indicated an interest in purchasing an aggregate of up to approximately $40.0 million in shares of our common stock in this offering at the initial public offering price and on the same terms as the other purchasers in this offering. However, because indications of interest are not binding agreements or commitments to purchase, these investors may determine to purchase fewer shares than they indicate an interest in purchasing or not to purchase any shares in this offering. It is also possible that these investors could indicate an interest in purchasing more shares of our common stock. In addition, the underwriters could determine to sell fewer shares to any of these investors than the investors indicate an interest in purchasing or not to sell any shares to these investors. The foregoing discussion and table do not reflect any potential purchase by these stockholders.

The foregoing tables and calculations exclude:

- 783,341 shares of our common stock issuable upon exercise of stock options outstanding under our 2007 Stock Option and Incentive Plan (2007 Plan), as amended, at a weighted average exercise price of $1.32 per share;
- 582,582 shares of our common stock issuable upon the exercise of stock options granted after March 31, 2016 at a weighted-average exercise price of $4.39 per share;
- 1,999,998 shares of redeemable preferred stock (convertible into 137,930 shares of common stock) issued pursuant to the exercise of preferred stock warrants after March 31, 2016;
- 52,948 shares of common stock reserved for issuance pursuant to future awards under our 2007 Plan, which will become available for issuance under our 2016 Plan upon the completion of this offering;
- 1,200,000 shares of common stock reserved, subject to increase on an annual basis, reserved for future issuance pursuant to our 2016 Plan, which will become effective upon completion of this offering as well as any automatic increases in the number of shares of common stock reserved for future issuance under this benefit plan; and

- 150,000 shares of our common stock reserved for future issuance under our 2016 ESPP, which will become effective upon completion of this offering, as well as any automatic increases in the number of shares of common stock reserved for future issuance under this benefit plan.

If the underwriters exercise their option to purchase additional shares of our common stock in full:

- the percentage of shares of common stock held by existing stockholders will decrease to approximately 56.8% of the total number of shares of our common stock outstanding after this offering; and
- the number of shares held by new investors will increase to 6,710,250, or approximately 43.2% of the total number of shares of our common stock outstanding after this offering.

SELECTED CONSOLIDATED FINANCIAL DATA

The following selected consolidated statements of operations data for the years ended December 31, 2014 and 2015 and the consolidated balance sheet data as of December 31, 2014 and 2015 have been derived from our audited consolidated financial statements included elsewhere in this prospectus. The selected consolidated statements of operations data for the three months ended March 31, 2015 and 2016, and the summary consolidated balance sheet data as of March 31, 2016, are derived from our unaudited interim condensed consolidated financial statements and related notes included elsewhere in this prospectus. Our unaudited interim condensed consolidated financial statements were prepared on the same basis as our audited consolidated financial statements and include, in our opinion, all adjustments, consisting of normal recurring adjustments that we consider necessary for a fair statement of the financial information set forth in those financial statements. Our historical results are not necessarily indicative of our future results and our interim results for the three months ended March 31, 2016 are not necessarily indicative of results to be expected for the full year ending December 31, 2016, or any other period. You should read the following selected consolidated financial data below in conjunction with "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our consolidated financial statements and related notes included elsewhere in this prospectus.

	Year Ended December 31,		Three Months Ended March 31,	
	2014	2015	2015	2016
	(In thousands, except share and per share data)			
Consolidated Statements of Operations Data:				
Operating expenses:				
Research and development	$ 7,459	$ 11,831	$ 2,183	$ 5,625
General and administrative	1,860	2,963	506	1,415
Total operating expenses	9,319	14,794	2,689	7,040
Loss from operations	(9,319)	(14,794)	(2,689)	(7,040)
Interest income	16	19	1	12
Change in fair value of redeemable convertible preferred stock tranche and warrant liabilities	(1,769)	(83)	(9)	(4,719)
Net loss	$ (11,072)	$ (14,858)	$ (2,697)	$ (11,747)
Net loss attributable to common stockholders[(1)]	$ (11,218)	$ (14,933)	$ (2,697)	$ (11,787)
Net loss per share attributable to common stockholders, basic and diluted[(1)]	$ (49.38)	$ (59.32)	$ (11.75)	$ (40.96)
Weighted-average shares used to compute net loss per share attributable to common stockholders, basic and diluted[(1)]	227,197	251,717	229,483	287,800
Pro forma net loss per share, basic and diluted (unaudited)[(1)]		$ (3.57)		$ (1.91)
Pro forma weighted-average shares used to compute net loss per share, basic and diluted (unaudited)[(1)]		4,313,032		5,884,892

(1) See Notes 2, 13, and 14 to our audited consolidated financial statements and Note 12 to our unaudited interim condensed consolidated financial statements included elsewhere in this prospectus for an explanation of the calculations of our basic and diluted net loss per share attributable to common stockholders, pro forma net loss per common share, and the weighted-average number of shares used in the computation of the per share amounts.

	As of December 31,		As of March 31,
	2014	2015	2016
	(In thousands)		
Consolidated Balance Sheet Data:			
Cash, cash equivalents and available-for-sale securities	$ 9,324	$ 11,923	$ 29,022
Working capital	8,563	11,080	26,467
Total assets	10,328	14,845	31,856
Convertible redeemable convertible preferred stock tranche liability	—	1,643	—
Convertible redeemable convertible preferred stock warrant liability	1,023	480	1,005
Convertible redeemable convertible preferred stock	20,576	36,996	65,361
Accumulated deficit	(12,558)	(27,416)	(39,162)
Total stockholders' deficit	(12,621)	(27,400)	(38,980)

MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following discussion and analysis of our financial condition and results of operations together with the section entitled "Selected Consolidated Financial Data" and our consolidated financial statements and related notes included elsewhere in this prospectus. This discussion and other parts of this prospectus contain forward-looking statements that involve risks and uncertainties, such as our plans, objectives, expectations, intentions and beliefs. Our actual results could differ materially from those discussed in these forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those identified below and those discussed in the section entitled "Risk Factors" included elsewhere in this prospectus.

Overview

We are a clinical-stage biopharmaceutical company with a proprietary technology platform focused on discovering and developing peptide-based new chemical entities (NCEs) to address significant unmet medical needs. Our primary focus is on developing first-in-class peptide drugs that specifically target biological pathways also targeted by currently marketed injectable antibody drugs. Compared to injectable antibody drugs, our oral peptides offer targeted delivery to the gastrointestinal (GI) tissue compartment, potential for improved safety due to minimal exposure in the blood, improved convenience and compliance due to oral delivery, and the opportunity for earlier introduction of targeted therapy for inflammatory bowel disease (IBD). Our initial lead product candidates, PTG-100 and PTG-200, are based on this approach, and we believe have the potential to transform the existing treatment paradigm for IBD, a GI disease consisting primarily of ulcerative colitis (UC) and Crohn's disease (CD).

PTG-100 is a potential first-in-class oral, alpha-4-beta-7 ($\alpha4\beta7$) integrin-specific antagonist peptide product candidate which has now completed a Phase 1 clinical trial in normal healthy volunteers (NHVs). Integrins are T cell receptors that facilitate migration of inflammatory cells into the GI tissue. An integrin antagonist peptide is a small molecule designed to block this migration, which is a hallmark of IBD. In our Phase 1 clinical trial, we have established pharmacological proof-of-concept (POC) based on pharmacodynamic (PD) indicators. We plan to initiate a Phase 2b clinical trial in moderate-to-severe UC patients by the end of the fourth quarter of 2016. The $\alpha4\beta7$ integrin is targeted by currently marketed injectable antibody drugs and the integrin pathway is considered to be one of the most specific biological mechanisms for IBD. Our second lead product candidate, PTG-200, is a potential first-in-class oral Interleukin-23 receptor (IL-23R) antagonist being developed initially for moderate-to-severe CD. Interleukin-23 is a protein produced by white blood cells that regulates inflammatory and immune functions. PTG-200 is currently in Investigational New Drug (IND) enabling studies, and we plan to initiate a Phase 1 clinical trial in 2017. Blocking of the integrin and Interleukin 23 (IL-23) pathways has led to FDA approved injectable antibody drugs for chronic inflammatory diseases, including IBD and psoriasis, respectively.

We believe PTG-100 and PTG-200 have the potential to transform the existing IBD treatment paradigm because they offer significant advantages over injectable antibody drugs. These complementary assets target different pathways, and potentially offer improved convenience and patient compliance, and improved safety and tolerability compared to currently approved injectable antibody drugs. We believe these potential advantages could allow our products to replace and expand the IBD market beyond the moderate-to-severe IBD patient population currently treated by injectable antibody drugs.

Our novel peptides have potential applicability in a wide range of therapeutic areas in addition to GI diseases. Our first product candidate beyond IBD is PTG-300, an injectable hepcidin mimetic, which is currently in pre-clinical development. PTG-300 has potential utility for the treatment of iron overload disorders, such as transfusion-dependent β-Thalassemia, hereditary hemochromatosis (HH) and sickle cell disease (SCD), each of which may qualify for orphan designation.

As of March 31, 2016, our cash, cash equivalents and available-for-sale securities was $29.0 million. In March 2016, we closed the second tranche of our Series C redeemable convertible preferred stock and obtained $22.5 million in net proceeds.

We have not generated any revenue from product sales and we do not currently have any products approved for commercialization. We have never been profitable and have incurred net losses in each year since inception. Our net losses were $11.1 million and $14.9 million for the years ended December 31, 2014 and 2015, respectively. Our net losses were $2.7 million and $11.7 million for the three months ended March 31, 2015 and 2016, respectively. As of March 31, 2016, we had an accumulated deficit of $39.2 million. Substantially all of our net losses have resulted from costs incurred in connection with our research and development programs and from general and administrative costs associated with our operations.

We expect to incur substantial expenditures in the foreseeable future for the advancement of our two lead product candidates and the development of our technology platform. Specifically, we expect to continue to incur substantial expenses in connection with our planned Phase 2b clinical trial for PTG-100, IND-enabling studies and initiation of a Phase 1 clinical trial for PTG-200, IND-enabling studies for PTG-300, and any additional clinical trials that we may conduct for our product candidates. We will need substantial additional funding to support our operating activities as we advance PTG-100, PTG-200, PTG-300 and other potential product candidates through clinical development, seek regulatory approval and prepare for, and if approved, proceed to commercialization. Adequate funding may not be available to us on acceptable terms, or at all.

Components of Our Results of Operations

Research and Development Expenses

Research and development expenses represent costs incurred to conduct research, such as the discovery and development of our product candidates. We recognize all research and development costs as they are incurred.

Research and development expenses consist primarily of the following:

- expenses incurred under agreements with clinical study sites that conduct research and development activities on our behalf;
- employee-related expenses, which include salaries, benefits and stock-based compensation;
- laboratory vendor expenses related to the preparation and conduct of pre-clinical, non-clinical, and clinical studies;
- costs related to production of clinical supplies and non-clinical materials, including fees paid to contract manufacturers and clinical research organizations;
- license fees; and
- facilities and other allocated expenses, which include expenses for rent and maintenance of facilities, depreciation and amortization expense and other supplies.

We recognize the funds from research and development grants as a reduction of research and development expense when the related research costs are incurred. In addition, we recognize the funds related to Australian Research and Development Tax Incentive that are not subject to refund provisions as a reduction of research and development expense. The amounts are determined on a cost reimbursement basis and as the incentive is related to our research and development expenditures and is non-refundable regardless of whether any Australian tax is owed, the amounts have been recorded as a reduction of research and development expenses. These Australian Research and Development Tax Incentives are recognized when there is reasonable assurance that the incentive will be received, the relevant expenditure has been incurred, and the amount of the consideration can be reliably measured.

We allocate direct costs incurred to product candidates when they enter into clinical development. For product candidates in clinical development, we allocate research and development salaries, benefits, stock-based compensation expense and indirect costs to our product candidates on a program-specific basis, and we include these costs in the program-specific expenses. Program-specific expenses are unallocated when the current clinical expenses are incurred for our early stage research and drug discovery projects, our internal resources, employees and infrastructure are not tied to any one research or drug discovery project and are typically deployed across multiple projects. As such, we do not maintain information regarding these costs incurred for the early stage research and drug discovery programs on a project-specific basis prior to the clinical development stage.

The following table shows our research and development expenses incurred during the respective periods:

	Year Ended December 31,		Three Months Ended March 31,	
	2014	2015	2015	2016
	(In thousands)			
Clinical development expense—PTG-100	$ —	$ 1,563	$ —	$4,016
Pre-clinical and discovery research expense	8,036	11,159	2,283	2,188
Less: Reimbursement of expenses under grants and incentives	(577)	(891)	(100)	(579)
Total research and development expenses	$7,459	$11,831	$2,183	$5,625

We expect our research and development expenses will increase as we progress our product candidates, advance our discovery research projects into the pre-clinical stage and continue our early stage research. The process of conducting research, identifying potential product candidates and conducting pre-clinical and clinical trials necessary to obtain regulatory approval is costly and time consuming. We may never succeed in achieving marketing approval for our product candidates. The probability of success of the product candidates may be affected by numerous factors, including pre-clinical data, clinical data, competition, manufacturing capability and commercial viability. As a result, we are unable to determine the duration and completion costs of our research and development projects or when and to what extent we will generate revenue from the commercialization and sale of any of our product candidates.

General and Administrative Expenses

General and administrative expenses consist of personnel costs, allocated facilities costs and other expenses for outside professional services, including legal, human resources, audit and accounting services. Personnel costs consist of salaries, benefits and stock-based compensation. Allocated expenses consist of expenses for rent and maintenance of facilities, depreciation and amortization expense and other supplies. We expect to incur additional expenses as a result of operating as a public company, including expenses related to compliance with the rules and regulations of the Securities and Exchange Commission, and those of any national securities exchange on which our securities are traded, additional insurance expenses, investor relations activities and other administrative and professional services.

Interest Income

Interest income consists of interest earned on our cash, cash equivalents and available-for-sale securities.

Change in Fair Value of Redeemable Convertible Preferred Stock Tranche and Warrant Liabilities

In connection with our Series B and Series C redeemable convertible preferred stock financings we were obligated to sell additional shares of Series B and Series C redeemable convertible preferred stock in subsequent closings, in each case, contingent upon the achievement of certain development milestones or upon the approval of the investors. We recorded this redeemable convertible preferred stock tranche liability incurred as a

derivative financial instrument liability at the fair value on the date of issuance, and we remeasure the liability on each subsequent balance sheet date. In addition, in connection with the issuance of our Series B redeemable convertible preferred stock financing, we issued freestanding warrants to purchase shares of Series B redeemable convertible preferred stock. We account for these warrants as a liability in our consolidated financial statements because the underlying instrument into which the warrants are exercisable contains redemption provisions that are outside our control.

Change in fair value of redeemable convertible preferred stock tranche and warrant liabilities consists of the remeasurement of the fair value of financial liabilities related to our obligation to sell additional redeemable convertible preferred stock shares in subsequent closings contingent upon the achievement of certain development milestones or approval of investors and warrants for the purchase of redeemable convertible preferred stock.

Critical Accounting Policies and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with United States generally accepted accounting principles. The preparation of these consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the consolidated financial statements, as well as the reported revenue generated and expenses incurred during the reporting periods. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. We believe that the accounting policies discussed below are critical to understanding our historical and future performance, as these policies relate to the more significant areas involving management's judgments and estimates.

Accrued Research and Development Costs

We record accrued expenses for estimated costs of our research and development activities conducted by third-party service providers, which include the conduct of pre-clinical studies and clinical trials and contract manufacturing activities. We record the estimated costs of research and development activities based upon the estimated amount of services provided but not yet invoiced, and include these costs in accrued liabilities in the consolidated balance sheets and within research and development expense in the consolidated statement of operations. These costs are a significant component of our research and development expenses. We record accrued expenses for these costs based on factors such as estimates of the work completed and in accordance with agreements established with these third-party service providers.

We estimate the amount of work completed through discussions with internal personnel and external service providers as to the progress or stage of completion of the services and the agreed-upon fee to be paid for such services. We make significant judgments and estimates in determining the accrued balance in each reporting period. As actual costs become known, we adjust our accrued estimates. Although we do not expect our estimates to be materially different from amounts actually incurred, our understanding of the status and timing of services performed, the number of patients enrolled and the rate of patient enrollment may vary from our estimates and could result in us reporting amounts that are too high or too low in any particular period. Our accrued expenses are dependent, in part, upon the receipt of timely and accurate reporting from clinical research organizations and other third-party service providers. To date, there have been no material differences from our accrued expenses to actual expenses.

Redeemable Convertible Preferred Stock Warrant Liability

We have issued freestanding warrants to purchase shares of redeemable convertible preferred stock in connection with the issuance of our Series B redeemable convertible preferred stock financing. We account for these warrants as a liability in our consolidated financial statements because the underlying instrument into which the warrants are exercisable contains redemption provisions that are outside our control.

The fair value of the warrants at the issuance date and December 31, 2014 and 2015 was determined using a one-step binomial lattice model in combination with the option pricing model. The fair value of the warrants outstanding as of March 31, 2016 was determined using a hybrid method of the option pricing model and the probability-weighted expected return method (PWERM). The warrants are re-measured at each financial reporting period with any changes in fair value being recognized in the consolidated statements of operations. We will continue to adjust the liability for changes in fair value until the earlier of (i) exercise of the warrants, (ii) conversion of warrants to purchase common stock, or (iii) expiration of the warrants. All unexercised warrants expired on May 10, 2016.

Redeemable Convertible Preferred Stock Tranche Liability

We recorded the redeemable convertible preferred stock tranche liability incurred in connection with our Series B and Series C redeemable convertible preferred stock as a derivative financial instrument liability at the fair value on the date of issuance, and we remeasure the liability on each subsequent balance sheet date. The Series B and Series C redeemable convertible preferred stock liability stems from our initial sale of Series B and Series C redeemable convertible preferred stock in connection with which we were obligated to sell additional shares in subsequent closings contingent upon the achievement of certain development milestones and approval from the investors. The subsequent closings were deemed to be freestanding financial instruments that were outside of our control. The changes in fair value are recognized as a gain or loss in the consolidated statements of operations and the liability is remeasured at each reporting period and settlement of the related tranche closing. We estimated the fair value of this liability using a one-step binomial lattice model in combination with the option pricing model that include assumptions of probability of achievement of the development milestones or funding of the financing, stock price, expected term and risk-free interest rate. The tranche closing of the Series B redeemable convertible preferred stock occurred in August 2014, so there is no derivative liability as of December 31, 2014, and there will be no additional remeasurement through the consolidated statement of operations in future periods. The Series C redeemable convertible preferred stock tranche liability was recorded upon the closing of the first tranche of the Series C redeemable convertible preferred stock in July 2015 and will be remeasured at the end of each reporting period until the obligation is settled or expires upon the earlier of (i) a deemed liquidation event, or (ii) the consummation of a firm commitment underwritten public offering. In March 2016, upon closing of the second tranche of the Series C redeemable convertible preferred stock, the fair value of the tranche liability was remeasured using a hybrid method of the option pricing model and PWERM and the liability was reclassified to redeemable convertible preferred stock.

Stock-Based Compensation

We recognize compensation costs related to stock options granted to employees based on the estimated fair value of the awards on the date of grant, net of estimated forfeitures. We estimate the grant date fair value, and the resulting stock-based compensation expense, using the Black-Scholes option-pricing model. The grant date fair value of the stock-based awards is generally recognized on a straight-line basis over the requisite service period, which is generally the vesting period of the respective awards.

The Black-Scholes option-pricing model requires the use of highly subjective assumptions which determine the fair value of stock-based awards. These assumptions include:

Expected Term— Our expected term represents the period that our stock-based awards are expected to be outstanding and is determined using the simplified method (based on the mid-point between the vesting date and

the end of the contractual term). We have very limited historical information to develop reasonable expectations about future exercise patterns and post-vesting employment termination behavior for our stock option grants.

Expected Volatility— Since we are privately held and do not have any trading history for our common stock, the expected volatility was estimated based on the average volatility for comparable publicly traded biopharmaceutical companies over a period equal to the expected term of the stock option grants. The comparable companies were chosen based on their similar size, stage in the life cycle, or area of specialty.

Risk-Free Interest Rate—The risk-free interest rate is based on the U.S. Treasury zero coupon issues in effect at the time of grant for periods corresponding with the expected term of option.

Expected Dividend—We have never paid dividends on our common stock and have no plans to pay dividends on our common stock. Therefore, we used an expected dividend yield of zero.

In addition to the Black-Scholes assumptions, we estimate our forfeiture rate based on an analysis of our actual forfeitures and will continue to evaluate the adequacy of the forfeiture rate based on actual forfeiture experience, analysis of employee turnover behavior, and other factors. The impact from any forfeiture rate adjustment would be recognized in full in the period of adjustment and if the actual number of future forfeitures differs from our estimates, we might be required to record adjustments to stock-based compensation in future periods.

For the years ended December 31, 2014 and 2015, stock-based compensation expense was $42,000 and $99,000, respectively. For the three months ended March 31, 2015 and 2016, stock-based compensation expense was $19,000 and $56,000, respectively. As of March 31, 2016, we had $0.4 million of total unrecognized stock-based compensation costs, net of estimated forfeitures, which we expect to recognize over a weighted-average period of 3.0 years.

Historically, for all periods prior to this initial public offering, the fair values of the shares of common stock underlying our share-based awards were estimated on each grant date by our board of directors. In order to determine the fair value of our common stock underlying option grants, our board of directors considered, among other things, contemporaneous valuations of our common stock prepared by an unrelated third-party valuation firm in accordance with the guidance provide by the American Institute of Certified Public Accountants Practice Guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*. Given the absence of a public trading market for our common stock, our board of directors exercised reasonable judgment and considered a number of objective and subjective factors to determine the best estimate of the fair value of our common stock, including our stage of development; progress of our research and development efforts; the rights, preferences and privileges of our preferred stock relative to those of our common stock; equity market conditions affecting comparable public companies and the lack of marketability of our common stock.

For valuations after the completion of this offering, our board of directors will determine the fair value of each share of underlying common stock based on the closing price of our common stock as reported on the date of grant.

The intrinsic value of all outstanding options as of March 31, 2016 was $8.4 million based on the estimated fair value of our common stock of $12.00 per share, the midpoint of the price range set forth on the cover page of this prospectus.

Income Taxes

We use the asset and liability method of accounting for income taxes. Under this method, deferred tax assets and liabilities are determined based on the differences between the financial reporting and the tax bases of assets and liabilities and are measured using the enacted tax rates and laws that will be in effect when the differences are expected to reverse. We assess the likelihood that the resulting deferred tax assets will be realized. A valuation allowance is provided when it is more likely than not that some portion or all of a deferred tax asset will not be realized.

As of December 31, 2015, our total gross deferred tax assets were $10.6 million. Due to our lack of earnings history and uncertainties surrounding our ability to generate future taxable income, the net deferred tax assets have been fully offset by a valuation allowance. The deferred tax assets were primarily comprised of federal and state tax net operating loss and tax credit carryforwards. As of December 31, 2015, our net operating loss carryforwards for Federal income tax purposes of $20.0 million which are available to offset future taxable income, if any, through 2033 and net operating loss carryforwards for state income tax purposes of approximately $9.4 million which are available to offset future taxable income, if any, through 2033. As of December 31, 2015, we also had accumulated Australian tax losses of $8.7 million available for carry forward against future earnings, which under relevant tax laws do not expire but may not be available under certain circumstances.

Utilization of the net operating loss carryforwards may be subject to a substantial annual limitation due to ownership changes that may have occurred or that could occur in the future, as required by Section 382 of the Internal Revenue Code of 1986 (Code), and similar state provisions. These ownership change limitations may limit the amount of net operating loss carryforwards and other tax attributes that can be utilized annually to offset future taxable income and tax, respectively. In general, an "ownership change" as defined by Section 382 of the Code results from a transaction or series of transactions over a three-year period resulting in an ownership change of more than 50 percentage points (by value) of the outstanding stock of a company by certain stockholders. Since our formation, we have raised capital through the issuance of capital stock on several occasions, which separately or combined with the purchasing stockholders' subsequent disposition of those shares, may have resulted in such ownership changes, or could result in ownership changes in the future.

Results of Operations

Comparison of the three months ended March 31, 2015 and 2016

	Three Months Ended March 31,		Dollar Change	% Change
	2015	2016		
	(Dollars in thousands)			
Operating expenses:				
Research and development	$ 2,183	$ 5,625	$ 3,442	158
General and administrative	506	1,415	909	180
Total operating expenses	2,689	7,040	4,351	162
Loss from operations	(2,689)	(7,040)	(4,351)	162
Interest income	1	12	11	*
Change in fair value of redeemable convertible preferred stock tranche and warrant liabilities	(9)	(4,719)	(4,710)	*
Net loss	$(2,697)	$(11,747)	$(9,050)	336

* Percentage not meaningful

Research and Development Expenses

Research and development expenses increased $3.4 million, or 158%, from $2.2 million for the three months ended March 31, 2015 to $5.6 million for the three months ended March 31, 2016. The increase was due to an increase of $1.2 million related to increased contract manufacturing activities for PTG-100 clinical trials, an increase of $1.8 million in PTG-100 Phase 1 clinical trials and other related studies, an increase of $0.4 million in salaries and employee-related expenses due to an increase in headcount, an increase of $0.3 million due to achieving certain development milestones in a prior collaboration agreement related to the initiation of pre-clinical development studies on PTG-300, and an increase of $0.2 million in costs to third party consultants. The

increases were partially offset by an increase of $0.5 million in government grants recognized as a reduction of research and development expenses, primarily due to the increase in our Australia research and development tax incentive grant and funds earned under the Small Business Innovation Research grant award obtained in 2015.

General and Administrative Expenses

General and administrative expenses increased $0.9 million, or 180%, from $0.5 million for the three months ended March 31, 2015, to $1.4 million for the three months ended March 31, 2016. The increase was due to an increase of $0.7 million in professional service fees and an increase of $0.2 million in salaries and employee-related expenses due to an increase in headcount to support the growth of our operations.

Change in Fair Value of Redeemable Convertible Preferred Stock Tranche and Warrant Liabilities

The change in estimated fair value associated with redeemable convertible preferred stock tranche liability and warrant liability increased $4.7 million from a charge of $9,000 for the three months ended March 31, 2015 to a charge of $4.7 million for the three months ended March 31, 2016, due to the fair value remeasurement of the outstanding mark to market liabilities. We issued the shares under our Series C obligation in March 2016, and accordingly, we no longer have an obligation as of that date. In April 2016, approximately half of the warrants for the purchase of redeemable preferred stock were exercised and the remaining half expired in May 2016. Accordingly, we will no longer be remeasuring the warrant liability as of those dates.

Comparison of the years ended December 31, 2014 and 2015

	Year Ended December 31,		Dollar Change	% Change
	2014	2015		
	(Dollars in thousands)			
Operating expenses:				
Research and development	$ 7,459	$ 11,831	$ 4,372	59
General and administrative	1,860	2,963	1,103	59
Total operating expenses	9,319	14,794	5,475	59
Loss from operations	(9,319)	(14,794)	(5,475)	59
Interest income	16	19	3	19
Change in fair value of redeemable convertible preferred stock tranche and warrant liabilities	(1,769)	(83)	1,686	(95)
Net loss	$(11,072)	$(14,858)	$(3,786)	34

Research and Development Expenses

Research and development expenses increased $4.4 million, or 59%, from $7.5 million for the year ended December 31, 2014 to $11.8 million for the year ended December 31, 2015. The increase was due to an increase of $2.8 million in pre-clinical activities for our product candidates, an increase of $0.8 million in PTG-100 Phase 1 clinical trials, which were incurred primarily in the fourth quarter of 2015, an increase of $0.6 million related to contract manufacturing activities, an increase of $0.5 million in salaries and employee-related expenses due to an increase in headcount and an increase of $0.1 million in costs to third party consultants primarily related to research and development activities for PTG-100. The increases were partially offset by an increase of $0.4 million in government grants recognized as a reduction to research and development expenses, primarily due to the increase in Australia research and development tax incentive grant and the Small Business Innovation Research grant award obtained in 2015.

General and Administrative Expenses

General and administrative expenses increased $1.1 million, or 59%, from $1.9 million for the year ended December 31, 2014, to $3.0 million for the year ended December 31, 2015. The increase was due to an increase of $0.5 million in salaries and employee-related expenses due to an increase in headcount, an increase of $0.5 million in professional services fees, primarily for patent related matters and an increase of $0.1 million in facility-related costs due to the increase in our leased facility space.

Change in Fair Value of Redeemable Convertible Preferred Stock Tranche and Warrant Liabilities

The change in estimated fair value associated with redeemable convertible preferred stock tranche liability and warrant liability decreased $1.7 million, or 95%, from a charge of $1.8 million for the year ended December 31, 2014 to a charge of $0.1 million for the year ended December 31, 2015, was due to the fair value remeasurement of the outstanding mark to market liabilities. We issued the shares under our Series B obligation in August 2014, and accordingly, we no longer have an obligation as of that date. However, we will continue to mark to market our Series C obligation until March 2016 when we issued the additional shares under our Series C obligation.

Liquidity and Capital Resources

Liquidity and Capital Expenditures

Since inception through March 31, 2016, our operations have been financed primarily by net proceeds of $66.6 million from the sale of shares of our convertible preferred stock. As of March 31, 2016, we had $29.0 million of cash, cash equivalents, and available-for-sale securities and an accumulated deficit of $39.2 million.

Our primary uses of cash are to fund operating expenses, primarily research and development expenditures. Cash used to fund operating expenses is impacted by the timing of when we pay these expenses, as reflected in the change in our outstanding accounts payable and accrued expenses.

We believe, based on our current operating plan and expected expenditures, that our existing cash, cash equivalents, available-for-sale securities and the net proceeds from this offering will be sufficient to meet our anticipated cash and capital expenditure requirements for at least the next 18 months. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we currently expect. Specifically, we expect to incur substantial expenses in connection with our planned Phase 2b clinical trial for PTG-100, our IND-enabling studies and planned clinical trial for PTG-200 and IND-enabling studies for PTG-300 and any other clinical trials that we may conduct. Furthermore, if our planned pre-clinical and clinical trials are successful, or our other product candidates enter clinical trials or advance beyond the discovery stage, we will need to raise additional capital in order to further advance our product candidates towards regulatory approval. We will continue to require additional financing to advance our current product candidates through clinical development, to develop, acquire or in-license other potential product candidates and to fund operations for the foreseeable future. We will continue to seek funds through equity or debt financings, collaborative or other arrangements with corporate sources, or through other sources of financing. We anticipate that we will need to raise substantial additional capital, the requirements of which will depend on many factors, including:

- the progress, timing, scope, results and costs of our pre-clinical studies and clinical trials for our product candidates, including the ability to enroll patients in a timely manner for our clinical trials;
- the costs of obtaining clinical and commercial supplies and any other product candidates we may identify and develop;
- our ability to successfully commercialize the product candidates we may identify and develop;

- the manufacturing, selling and marketing costs associated with our lead product candidates and any other product candidates we may identify and develop, including the cost and timing of expanding our sales and marketing capabilities;
- the amount and timing of sales and other revenues from our lead product candidates and any other product candidates we may identify and develop, including the sales price and the availability of adequate third-party reimbursement;
- the cash requirements of any future acquisitions or discovery of product candidates;
- the time and cost necessary to respond to technological and market developments;
- the extent to which we may acquire or in-license other product candidates and technologies;
- our ability to attract, hire and retain qualified personnel; and
- the costs of maintaining, expanding and protecting our intellectual property portfolio.

Adequate additional funding may not be available to us on acceptable terms, or at all. Any failure to raise capital as and when needed could have a negative impact on our financial condition and on our ability to pursue our business plans and strategies. Further, our operating plans may change, and we may need additional funds to meet operational needs and capital requirements for clinical trials and other research and development activities. If we do raise additional capital through public or private equity offerings, the ownership interest of our existing stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our stockholders' rights. If we raise additional capital through debt financing, we may be subject to covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. We currently have no credit facility or committed sources of capital. Because of the numerous risks and uncertainties associated with the development and commercialization of our product candidates, we are unable to estimate the amounts of increased capital outlays and operating expenditures associated with our current and anticipated product development programs.

The following table summarizes our cash flows for the periods indicated:

	Year Ended December 31,		Three Months Ended March 31,	
	2014	2015	2015	2016
	(In thousands)			
Cash used in operating activities	$(7,743)	$(14,385)	$(2,433)	$ (5,239)
Cash provided by (used in) investing activities	$ (299)	$ (8,264)	$ (5)	$ 7,147
Cash provided by financing activities	$ 9,003	$ 17,419	$ 2	$22,631

Cash Flows from Operating Activities

Cash used in operating activities for the three months ended March 31, 2016 was $5.2 million, consisting of a net loss of $11.7 million, which was offset by non-cash charges of $4.9 million and a net change of $1.6 million in our net operating assets and liabilities. The non-cash charges were primarily comprised of $4.2 million for the change in fair value of redeemable convertible preferred stock tranche liability, $0.5 million for the change in fair value of convertible preferred stock warrant liability, $0.1 million for depreciation and amortization expense and $0.1 million for stock-based compensation. The increase in our net operating assets and liabilities was due primarily to an increase of $1.2 million in our accounts payable and accrued liabilities related to an increase in research and development activities and a decrease of $0.9 million in prepaid and other current assets related to expensing of costs for research activities that occurred during the quarter, offset by a $0.5 million increase in the receivable related to the Australia research and development tax incentive.

Cash used in operating activities for the three months ended March 31, 2015 was $2.4 million, consisting of a net loss of $2.7 million, which was offset by non-cash charges of $0.1 million primarily for depreciation and amortization expense and a net change of $0.2 million in our net operating assets and liabilities due primarily to an increase in our accounts payable and prepaid expenses related to the increase in research and development activities.

Cash used in operating activities for the year ended December 31, 2015 was $14.4 million, consisting of a net loss of $14.9 million, which was partially offset by non-cash charges of $0.4 million and a net change of $0.1 million in our net operation assets and liabilities. The non-cash charges were primarily comprised of $0.6 million for the change in fair value of redeemable convertible preferred stock tranche liability, $0.2 million for depreciation and amortization expense, $0.1 million for stock-based compensation, offset by gain of $0.5 million for the change in fair value of convertible preferred stock warrant liability. The change in our net operating assets and liabilities was due primarily to an increase of $1.8 million in our accounts payable and accrued liabilities related to an increase in research and development activities, offset by $1.5 million increase in cash used for prepaid and other current assets related to payments associated with clinical trials and studies and a $0.2 million increase in a receivable related to the Australia research and development tax incentive.

Cash used in operating activities for the year ended December 31, 2014 was $7.7 million, consisting of a net loss of $11.1 million, which was partially offset by non-cash charges primarily of $2.1 million and a net increase of $1.3 million in our net operation assets and liabilities. The non-cash charges were primarily comprised of $1.8 million for the change in fair value of our convertible preferred stock tranche and warrant liabilities and $0.3 million for depreciation and amortization expense. The change in our net operating assets and liabilities was due primarily to decrease of $0.6 million in prepaid expenses and other current assets related to payments for research and development activities, an increase of $0.4 million in our accounts payable and accrued liabilities related to an increase in research and development activities and a $0.3 million increase in receivable related to the Australia research and development tax incentive.

Cash Flows from Investing Activities

Cash provided by investing activities for the three months ended March 31, 2016 was $7.1 million, consisting of the proceeds from maturities of our available-for-sale securities of $7.4 million, which were partially offset by our purchase of property and equipment of $0.3 million. The purchase of property and equipment was primarily related to the expansion of our laboratory and related equipment.

Cash used in investing activities for the three months ended March 31, 2015 was related to our purchase of property and equipment of $5,000.

Cash used in investing activities for the years ended December 31, 2015, was $8.3 million, consisting of the purchase of available-for-sale securities of $7.9 million and our purchase of property and equipment of $0.4 million. The purchase of property and equipment was primarily related to the expansion of our laboratory and the purchase of related equipment.

Cash used in investing activities for the years ended December 31, 2014, was related to our purchase of property and equipment of $0.3 million. The purchase of property and equipment was primarily related to the expansion of our laboratory and the purchase of related equipment.

Cash Flows from Financing Activities

Cash provided by financing activities for the three months ended March 31, 2016 was $22.6 million was related to net proceeds of $22.5 million from the issuance of redeemable convertible preferred stock and proceeds of $0.1 million from the issuance of common stock upon exercise of stock options.

Cash provided by financing activities for the three months ended March 31, 2015 was related to proceeds of $2,000 from the issuance of common stock upon exercise of stock options.

Cash provided by financing activities for the years ended December 31, 2015 and 2014 was primarily related to proceeds from the issuance of redeemable convertible preferred stock of $17.4 million and $9.0 million, respectively.

Contractual Obligations and Other Commitments

The following table summarizes our contractual obligations as of December 31, 2015:

	Payments Due by Period				
Contractual Obligations:	**Less Than 1 Year**	**1 to 3 Years**	**3 to 5 Years**	**More Than 5 Years**	**Total**
			(In thousands)		
Operating lease obligations	$372	$402	$—	$—	$774
Total contractual obligations	$372	$402	$—	$—	$774

We enter into agreements in the normal course of business with contract research organizations for clinical trials and with vendors for pre-clinical studies and other services and products for operating purposes, which are cancelable at any time by us, generally upon 30 to 60 days prior written notice. These payments are not included in this table of contractual obligations.

In addition to the amounts set forth in the table above, we have certain obligations under licensing agreements with third parties contingent upon achieving various development, regulatory and commercial milestones. In October 2013, the collaboration program under our Research Collaboration and License Agreement with Zealand Pharma A/S (Zealand) was abandoned by Zealand. Pursuant to the terms of the agreement, we elected to assume the responsibility for the development and commercialization of the product candidate. Upon Zealand's abandonment, Zealand assigned to us certain intellectual property arising from the collaboration and also granted us an exclusive license to certain background intellectual property rights of Zealand that relate to the products assumed by us. Upon the nomination of PTG-300 as a development candidate, we owed Zealand a payment of $250,000, which has been recognized within research and development expense in our consolidated statement of operations for the three months ended March 31, 2016. If we initiate a Phase 1 clinical trial for PTG-300, we will pay Zealand an additional $250,000. We have the right, but not the obligation, to further develop and commercialize the product candidate and, if we successfully develop and commercialize PTG-300 without a partner, we will pay to Zealand up to an additional aggregate of $128.5 million for the achievement of certain development, regulatory and sales milestone events. In addition, we will pay to Zealand a low single digit royalty on worldwide net sales of the product. As the achievement and timing of these future milestone payments are not probable and estimable, such amounts have not been included on our consolidated balance sheets or in the contractual obligations table above.

Off-Balance Sheet Arrangements

We have not entered into any off-balance sheet arrangements and do not have any holdings in variable interest entities.

Quantitative and Qualitative Disclosures about Market Risk

We are exposed to market risks in the ordinary course of our business. These risks primarily include interest rate sensitivities.

We had $11.9 million and $29.0 million in cash, cash equivalents and available-for-sale securities as of December 31, 2015 and March 31, 2016, respectively. Cash and cash equivalents consist of cash and money market funds. Available-for-sale securities consist of corporate bonds and commercial paper. Such interest-earning instruments carry a degree of interest rate risk; however, historical fluctuations in interest income have not been significant. We had no outstanding debt as of March 31, 2016.

Approximately $0.6 million and $1.0 million of our cash balance is located in Australia as of December 31, 2015 and March 31, 2016, respectively. Our expenses, except those related to our Australian operations, are generally denominated in U.S. dollars. For our operations in Australia, the majority of the expenses are denominated in Australian dollars. To date, we have not had a formal hedging program with respect to foreign currency, but we may do so in the future if our exposure to foreign currency should become more significant. A 10% increase or decrease in current exchange rates would not have a material effect on our consolidated financial results.

JOBS Act Accounting Election

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. Under the JOBS Act, emerging growth companies can delay adopting new or revised accounting standards issued subsequent to the enactment of the JOBS Act until such time as those standards apply to private companies. We have irrevocably elected not to avail ourselves of this exemption from new or revised accounting standards, and, therefore, will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

Recent Accounting Pronouncements

In August 2014, the Financial Accounting Standards Board (FASB) issued ASU No. 2014-15, *Disclosure of Uncertainties About an Entity's Ability to Continue as a Going Concern*. ASU 2014-15 requires management to perform interim and annual assessments of an entity's ability to continue as a going concern within one year of the date the financial statements are issued and provides guidance on determining when and how to disclose going concern uncertainties in the financial statements. Certain disclosures will be required if conditions give rise to substantial doubt about an entity's ability to continue as a going concern. ASU 2014-15 applies to all entities and is effective for annual and interim reporting periods ending after December 15, 2016, with early adoption permitted. We are currently evaluating the effect the adoption of this standard will have, if any, on our consolidated financial statements.

In November 2015, FASB issued ASU No. 2015-17, *Income Taxes (Topic 740): Balance Sheet Classification of Deferred Taxes*, which is intended to simplify and improve how deferred taxes are classified on the balance sheet. The guidance in this ASU eliminates the current requirement to present deferred tax assets and liabilities as current and noncurrent in a classified balance sheet and now requires entities to classify all deferred tax assets and liabilities as noncurrent. The guidance is effective for annual periods beginning after December 15, 2016 and for interim periods within those annual periods though early adoption is permitted. We do not expect that the adoption of the guidance will have a material effect on our consolidated financial statements.

In February 2016, the FASB issued ASU No. 2016-02, *Leases* (Topic 842). Under the new guidance, (with the exception of short-term leases) at the commencement date, lessees will be required to recognize a lease liability and a right-of-use asset. Lessor accounting is largely unchanged, while lessees will no longer be provided with a source of off-balance sheet financing. Public business entities should apply the amendments in ASU 2016-02 for fiscal years beginning after December 15, 2018, including interim periods within those fiscal years (January 1, 2019, for us). Early application is permitted. Lessees (for capital and operating leases) must apply a modified retrospective transition approach for leases existing at, or entered into after, the beginning of the earliest comparative period presented in the financial statements. The modified retrospective approach would not require any transition accounting for leases that expired before the earliest comparative period presented. We are currently evaluating the impact that the standard will have on our consolidated financial statements.

In March 2016, the FASB issued ASU 2016-09 Compensation-Stock Compensation (Topic 718) Improvements to Employee Share-Based Payment Accounting, which is intended to simplify several aspects of the accounting for employee share-based payment transactions, including the income tax consequences, the determination of forfeiture rates, classification of awards as either equity or liabilities, and classification on the statement of cash flows. This ASU is effective for fiscal years and interim periods within those years beginning after December 15, 2016 and early adoption is permitted. We are currently evaluating the impact that the adoption of ASU 2016-09 will have on our consolidated financial statements and related disclosures.

BUSINESS

Overview

We are a clinical-stage biopharmaceutical company with a proprietary technology platform focused on discovering and developing peptide-based new chemical entities (NCEs) to address significant unmet medical needs. Our primary focus is on developing first-in-class oral peptide drugs that specifically target the same biological pathways also targeted by currently marketed injectable antibody drugs. Compared to injectable antibody drugs, our oral peptides offer targeted delivery to the gastrointestinal (GI) tissue compartment, potential for improved safety due to minimal exposure in the blood, improved convenience and compliance due to oral delivery and the opportunity for earlier introduction of targeted therapy for inflammatory bowel disease (IBD). Our initial lead product candidates, PTG-100 and PTG-200, are based on this approach and we believe they have the potential to transform the existing treatment paradigm for IBD, a GI disease consisting primarily of ulcerative colitis (UC), and Crohn's disease (CD).

PTG-100 is a potential first-in-class oral, alpha-4-beta-7 ($\alpha4\beta7$) integrin-specific antagonist peptide product candidate which has now completed a Phase 1 clinical trial in normal healthy volunteers (NHVs). Integrins are T cell receptors that facilitate migration of inflammatory cells into the GI tissue. An integrin antagonist peptide is a small molecule designed to block this migration, which is a hallmark of IBD. In our Phase 1 clinical trial, we have established pharmacological proof-of-concept (POC) based on pharmacodynamic (PD) indicators. We plan to initiate a Phase 2b clinical trial in moderate-to-severe UC patients by the end of the fourth quarter of 2016. The $\alpha4\beta7$ integrin is targeted by currently marketed injectable antibody drugs and the integrin pathway is considered to be one of the most specific biological mechanisms for IBD. Our second product candidate, PTG-200, is a potential first-in-class oral Interleukin 23 receptor (IL-23R) antagonist being developed initially for moderate-to-severe CD. Interleukin-23 is a protein produced, by white blood cells that regulates inflammatory and immune functions. PTG-200 is currently in Investigational New Drug (IND) enabling studies, and we plan to initiate a Phase 1 clinical trial in 2017. Blocking of the integrin and Interleukin 23 (IL-23) pathways has led to FDA approved injectable antibody drugs for chronic inflammatory diseases, including IBD and psoriasis, respectively.

IBD is a chronic inflammatory disease with significant unmet medical need, and a large and growing market with an estimated 1.6 million patients in the United States in 2013. As of 2008, annual direct treatment costs for patients with IBD in the United States were estimated to exceed $6.3 billion, with indirect costs estimated to be an additional $5.5 billion. In 2012, Global Data estimated that the UC and CD markets reached approximately $4.2 billion and $3.2 billion, respectively, across ten major markets, and Global Data estimates that these markets are expected to grow at a compound annual growth rate of approximately 3% to 5% through 2022. The current tumor necrosis factor-alpha (TNF-α) antibody drugs approved for moderate-to-severe IBD, Humira® and Remicade®, are both injectable. According to Global Data, the 2013 sales for Humira® and Remicade® for IBD were $3.4 billion in the United States. Approximately one third of IBD patients are non-responders to TNF-α antibody drugs and approximately another 30% to 40% become refractory within the first year of treatment. Additionally, TNF-α antibody drugs may predispose patients to an increased risk of serious infection and the development of anti-drug antibodies (ADAs), which over time can cause loss of drug response. Thus, while available treatments exist for moderate-to-severe IBD, there continues to be a significant medical need for efficacious, safer, and convenient treatments.

We believe PTG-100 and PTG-200 have the potential to transform the existing IBD treatment paradigm because they offer significant advantages over injectable antibody drugs. These complementary assets target different pathways, and potentially offer improved convenience, patient compliance, and safety and tolerability compared to currently approved injectable antibody drugs. We believe these potential advantages could allow our products to replace and expand the IBD market beyond the moderate-to-severe IBD patient population currently treated by injectable antibody drugs.

PTG-100 and PTG-200 are derived from our proprietary peptide technology platform. Peptide therapeutics represent a substantial and growing therapeutic class with more than 60 FDA approved drugs. Our platform enables

us to discover novel, structurally constrained peptides that retain certain key advantages of both oral and small molecule and injectable antibody drugs, while overcoming many of their limitations as therapeutic agents. Constrained peptides are rigid, well-folded structures typically formed by disulfide bonds that alleviate the fundamental instability inherent in traditional peptides, which cannot be delivered orally. Further, these constrained peptides are designed to bind to biological targets, including protein-protein interactions (PPI) targets, which are typically approached by antibodies since small molecules cannot bind effectively to these targets. It is estimated that up to 80% of all potential disease targets are not amenable to drug development by small molecules and have therefore traditionally been approached by injectable antibody drugs. The key differences between our constrained peptides, small molecules and antibody drugs are summarized in Figure 1 below.

Figure 1: Characteristics of Small Molecules vs. Constrained Peptides vs. Antibodies

	Small Molecules	Constrained Peptides	Antibodies
			
Molecular Size	~0.5 kDa	~1 to 3 kDa	~150 kDa
Route of Administration	Oral	Oral or Injectable	Injectable
Features	Do not bind to most PPI targets	High potency and selectivity against PPI targets	Expensive and inconvenient to administer

Our novel peptides have potential applicability in a wide range of therapeutic areas in addition to GI diseases. Our first product candidate beyond IBD is PTG-300, an injectable hepcidin mimetic, which is currently in pre-clinical development with completion of IND-enabling studies expected by the end of the first half of 2017. A hepcidin mimetic is a peptide that mimics the function of the natural hormone, hepcidin. PTG-300 has potential utility for the treatment of iron overload disorders, such as transfusion-dependent β-Thalassemia, hereditary hemochromatosis (HH) and sickle cell disease (SCD), each of which may qualify PTG-300 for orphan drug designation.

Our Pipeline

We will continue to leverage our proprietary peptide technology platform to discover and develop novel product candidates to treat diseases with significant unmet medical needs. The following table summarizes key information about our peptide product candidates to date:

			Development Status				
Program	**Dosing Form**	**Indication**	**Preclinical**	**Phase 1**	**Phase 2**	**Anticipated Milestones**	**Commercial Rights**
PTG-100 (α4β7 Antagonist)	Oral	IBD (Ulcerative Colitis)				Initiate Phase 2b Clinical Trial by the end of Q4 2016	Worldwide
PTG-200 (IL-23R Antagonist)	Oral	IBD (Crohn's Disease)				Initiate Phase 1 Clinical Trial in 2017	Worldwide
PTG-300 (Hepcidin Mimetic)	Injectable (Sub-Q)	Iron Overload Disorders				Initiate Phase 1 Clinical Trial in 2017	Worldwide

Our Product Candidates

PTG-100

PTG-100 has first-in-class potential as an oral, α4β7 integrin-specific antagonist for the treatment of IBD. The α4β7 integrin is considered to be one of the most GI-specific biological targets for IBD. It is a cell surface protein present on T cells that plays an important role in the trafficking of T cells to the GI tissue compartment by binding to MAdCAM-1, an extracellular protein that resides mostly in the GI vasculature.

We are leveraging several factors to inform and guide the clinical development of PTG-100 for the treatment of IBD. First, PTG-100 shares the same α4β7 integrin target as the injectable antibody drug vedolizumab, marketed as Entyvio®, for the treatment of moderate-to-severe UC and CD. Second, we utilized PD biomarker assays similar to those described in scientific publications used with Entyvio® and other antibodies in development as indicators of target engagement to establish POC in our Phase 1 clinical trial with PTG-100. These PD data include increases in receptor occupancy and decreases in receptor expression. We believe that we can utilize published information describing the development and regulatory path of Entyvio® and other approved antibody drugs for IBD to help inform the design of our clinical development studies.

We have completed extensive pre-clinical studies of PTG-100 in which we established pharmacological POC, including effects on T cell trafficking and mucosal healing similar to comparator α4β7 rodent antibody, DATK-32. Following the submission and approval of a Clinical Trial Notification (CTN) in Australia in December 2015, we initiated a Phase 1 clinical trial, comprised of three components: a single ascending dose (SAD) and multiple ascending dose (MAD) component, each of which evaluated safety, pharmacokinetics (PK), and PD-based POC in healthy subjects, using an oral liquid formulation of PTG-100. The trial also included a bridging component which compared the relative bioavailability and PD effects of the liquid formulation and a capsule formulation of PTG-100 that we intend to use in our Phase 2b clinical trial. The Phase 1 clinical trial was completed in June 2016. There were no serious adverse events reported in the Phase 1 clinical trial, and no dose-limiting toxicities were observed. All reported adverse events were of mild to moderate severity. There were no dose-dependent increases observed for any adverse events. The most frequent adverse events reported by subjects on PTG-100 were headache and upper respiratory tract infection. These events were also observed in subjects who took placebo. The preliminary maximally tolerated dose was established at 1,000 mg, the highest dose tested, for both single and multiple dosing, although no dose-limiting toxicities were observed at the 1,000 mg dose level. In addition, we observed dose-dependent PD effects, including target engagement and pharmacologic activity, similar to what was observed in the pre-clinical setting. Finally, we established the plasma exposure of the capsule formulation was lower than that of the liquid formulation at the same dose level. The PD effects (target engagement and pharmacologic activity) were highly similar between the two formulations, despite the lower plasma exposure of the capsule formulation. We believe this data will support the introduction of the capsule formulation in the Phase 2b clinical trial. We expect to have final unblinded data from the completed Phase 1 clinical trial by the end of the third quarter of 2016.

We plan to file an IND in the United States by the end of the third quarter of 2016 to support initiation of a global Phase 2b randomized, double-blinded, placebo-controlled dose-finding clinical trial by the end of the fourth quarter of 2016 to assess safety and efficacy of PTG-100 in approximately 260 moderate-to-severe UC patients. In this Phase 2b trial we plan to utilize the same capsule formulation that was used in the formulation bridging component of the Phase 1 clinical trial. The primary endpoint of our Phase 2b clinical trial is expected to be the induction of remission, which is consistent with the development of previously approved drugs for UC. We plan to develop PTG-100 initially for the treatment of moderate-to-severe UC, potentially followed by CD and pediatric IBD, the latter being an orphan indication.

PTG-200

Our second oral, GI-restricted peptide product candidate is PTG-200, a potential first-in-class IL-23R specific antagonist for the treatment of IBD. IL-23 is a member of the IL-12 family of pro-inflammatory

cytokines, which are proteins that regulate inflammatory and immune function and play a key role in the development of IBD. By blocking the IL-23 receptor with PTG-200 in the GI tissue compartment we expect to reduce inflammation while potentially minimizing the risk of systemic side effects due to its GI-restricted nature. The IL-23 pathway is targeted by the IL-12 and IL-23 antagonist infused antibody drug ustekinumab marketed as Stelara® for psoriasis and psoriatic arthritis. Stelara® has also recently reported positive Phase 3 clinical trial results in patients with moderate-to-severe CD.

We have completed pre-clinical POC studies for PTG-200, started IND-enabling studies, and plan to initiate a Phase 1 clinical trial in 2017. We plan to develop PTG-200 initially for the treatment of moderate-to-severe CD, potentially followed by UC and pediatric IBD, the latter being an orphan indication.

PTG-300

PTG-300 is an injectable hepcidin mimetic peptide that we are developing for the treatment of iron overload disorders, such as transfusion-dependent β-Thalassemia, HH and SCD, each of which may qualify for orphan drug designation. Hepcidin is a peptide hormone critical for regulating iron homeostasis. However, hepcidin has significant stability, potency and solubility limitations. We have discovered and developed PTG-300 as a stable, soluble, hepcidin mimetic that can potentially be more potent and more amenable for weekly or less frequent subcutaneous delivery compared to hepcidin. We plan to complete IND-enabling studies in by the end of the first half of 2017 and initiate a Phase 1 clinical trial in 2017.

Our Peptide Technology Platform

Our proprietary peptide technology platform is based on a series of tools and methods which allow us to discover and develop structurally novel oral or injectable peptides as potential product candidates. The platform utilizes these tools and techniques in an integrated and iterative manner in synergy with our deep-rooted knowledge in peptide chemistry, which allows us to arrive at a product with the desired potency, selectivity, oral or plasma stability, PK, and physicochemical properties. These tools and techniques include, but are not limited to, the following:

- *Molecular design tools and large virtual libraries of constrained scaffolds, collectively known as Vectrix™*: Allows for the *de novo* selection of peptide scaffolds as starting points against specific targets.
- *Random libraries and phage display techniques:* Allows for the discovery and optimization of peptide hits.
- *Oral stability assays: In vitro* and *ex vivo* assays and systems that simulate chemical and biological mechanisms, and physical barriers that constrained peptides must overcome for oral stability.
- *Medicinal peptide chemistry:* Allows optimization and refinement of potency, selectivity, oral stability and GI restriction.
- *In vivo pharmacology tools for GI restriction*: Tools to quantify compound concentrations and activity in various GI tissue compartments to develop oral products with minimal systemic exposure.

To date, our platform has generated two oral antagonist peptide candidates, PTG-100 and PTG-200, for IBD, and an injectable hepcidin peptide mimetic, PTG-300, for iron overload disorders, exemplifying our platform's reproducibility and broad scope. We will continue to use our technology platform to discover novel peptides against targets and diseases where oral small molecules or injectable biologics do not offer satisfactory outcomes to patients.

Our Strategy

Our goal is to become a leading biopharmaceutical company by discovering, developing and commercializing first-in-class peptide-based therapeutics that have the potential to transform current treatment paradigms for patients and address unmet medical needs. We are currently pursuing the development of oral peptides that specifically target a number of biological pathways that are also targeted by currently marketed injectable antibody drugs. The critical components of our strategy are as follows:

- **Advance our two lead oral, GI-restricted peptide product candidates, PTG-100 and PTG-200, in clinical development to evaluate the safety, PK, PD-based POC and efficacy in IBD patients.**
  - *PTG-100:* We completed our Phase 1 clinical trial of PTG-100. This clinical trial was designed to evaluate safety and tolerability, PK, and PD-based POC in NHVs, as well as evaluate the relative bioavailability of our capsule formulation compared to the liquid formulation. We plan to initiate a Phase 2b clinical trial of PTG-100 in patients with moderate-to-severe UC by the end of the fourth quarter of 2016.
  - *PTG-200:* We have commenced IND-enabling studies of PTG-200 and plan to initiate a Phase 1 clinical trial in 2017. PTG-200 will initially be developed as a targeted oral therapy for patients with moderate-to-severe CD.
- **Leverage our peptide technology platform to expand our differentiated peptide-based product pipeline across multiple therapeutic areas**.
  - *PTG-300:* We have initiated IND-enabling studies of PTG-300, a subcutaneous (SC), injectable hepcidin mimetic peptide that would be developed for iron overload disorders such as transfusion-dependent β-Thalassemia, HH, and SCD, each of which may qualify for orphan designation.
- **Opportunistically expand the value of our oral, GI-restricted peptide product candidates through co-development and regional partnerships.** For PTG-100 and PTG-200, we intend to retain key development and commercialization rights in the United States and build a commercial infrastructure; however, we will consider other strategic opportunities as they arise. We may decide to enter into co-development collaborations in select geographies where we believe a collaborator can bring additional regional development and/or commercial expertise in order to maximize the value of our oral, GI-restricted peptide product candidates.
- **Out-license non-core assets and structure research collaborations based on our proprietary peptide technology platform.** We continually review our internal research priorities and therapeutic focus and may decide to out-license non-core assets that arise from our platform. We may seek research collaborations that leverage the capabilities of our core technology platform, in order to monetize and expand upon the breadth of opportunities that may be uniquely accessible through our platform.
- **Protect and leverage our intellectual property portfolio and patents.** We believe that our intellectual property protection strategy, grounded in securing composition of matter patents on the NCEs developed using our technology platform, has best positioned us to gain broad and strong protection of our assets.
- **Leverage the drug discovery, development and commercialization expertise of our management team and network of scientific advisors and key opinion leaders.** We are led by a strong management team with deep experience in drug discovery and development, collaborations, operations and corporate finance. Our team has been involved in a broad spectrum of R&D activities leading to successful outcomes, including FDA approved and marketed drugs. We will continue to leverage the collective experience and talent of our management team, our network of leading scientific experts, and key opinion leaders (KOLs) to strategize and implement our development and commercialization strategy.

The Evolution of Antibody Drugs for Targeted Therapy and Their Limitations

Before the FDA approval of antibody drugs, chemically synthesized oral small molecules were the standard-of-care for the treatment of many diseases. However, small molecules are not capable of blocking most PPIs that underpin cellular processes frequently involved in numerous diseases. It is estimated that small molecules cannot be developed as drugs for the treatment of up to 80% of all identified potential disease targets. With the availability of antibody drugs, targeted therapy for many PPI-driven diseases became feasible.

In 2015, six of the top ten selling U.S. drugs were antibody drugs. In 2013, all approved antibody drugs generated approximately $75 billion in sales. More than 30 antibody drugs have now been approved by the FDA, including the IBD targeted therapy drugs Humira®, Remicade® and Entyvio®.

Despite their growing use, antibody drugs present several limitations for patients including, but not limited to, the following:

- *Injections or infusions are associated with significant patient burden.* Antibody drugs are large proteins that are not stable in the GI tissue compartment. As a consequence, antibody based therapies are administered primarily by injection or infusion into systemic circulation. Injections or infusions as a mode of delivery can increase patient burden including site reactions and systemic hypersensitivity, inconvenience, and needle anxiety and phobia, each of which may negatively affect patient compliance.
- *Antibody drugs may have significant safety issues.* Antibody drugs are typically administered at high concentrations in order to attain appropriate therapeutic levels at distal sites of a disease. High systemic exposure of immunomodulatory agents can increase the risks of use for patients:
  - *Elevated risk of serious or opportunistic infection, malignancy and severe hypersensitivity events.* Many antibody drugs are immunosuppressive, which may lead to increased risk of serious or opportunistic infection, such as tuberculosis, histoplasmosis and hepatitis B, or malignancy. Further, injection or infusion may increase the risk of severe hypersensitivity reactions including anaphylaxis.
  - *Long half-life resulting in delayed clearance from the bloodstream.* Antibody drugs are large molecules engineered to have long half-lives and to circulate in the bloodstream for extended periods of time. This longevity can be potentially problematic for patients who experience adverse reactions and cannot readily eliminate the drug from their systems.
  - *Immunogenicity reactions can lead to loss of response or possible safety risks.* Antibody drugs may induce natural immunogenic responses from the body including the introduction of ADAs. These ADAs can neutralize the action of the therapeutic antibody either by enhancing its clearance or blocking its function, either of which can result in loss of therapeutic response. ADAs can cause immunogenic reactions in patients leading to possible adverse events, frequently necessitating drug withdrawal.
- *Antibody drugs are expensive*. Compared to other classes of therapeutics, the complexity and size of antibody drugs can result in high manufacturing, storage and administration costs. To date, these costs have not been significantly reduced through the introduction of biosimilar drugs.

Our Solution for IBD: Oral, GI-Restricted Peptides

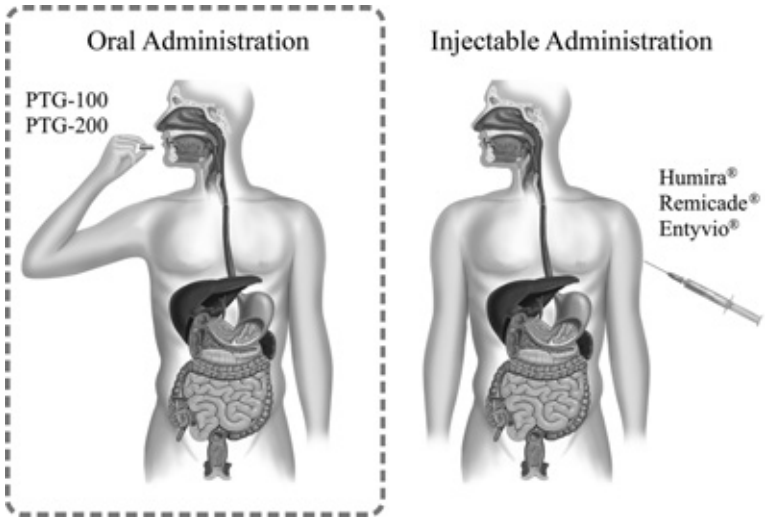
Our novel peptide therapeutics platform may provide important benefits over existing non-targeted small molecule, injectable antibody, and conventional peptide therapeutics. In addition, our platform represents a major step forward in the evolution of peptides as therapeutics. Most of the more than 60 currently FDA approved peptides have unstructured shapes, leading to chemical and biological stability limitations, which confine their use to injectable drugs. In contrast, our peptide technology platform allows us to identify constrained peptides

that can serve as a starting point for discovery and development of oral, selective, and potent peptides. The well-folded conformation in our constrained peptides is typically derived by disulfide bonds, a structural feature inherent in many naturally occurring peptides. For the IBD targets of interest, the size and nature of our peptides is carefully selected and modified so as to acquire the desired potency and specificity, and also to restrict their presence to the GI tissue compartment when administered orally. These features translate to oral, GI-restricted, selective and potent peptide drug candidates with specific advantages compared to antibody drugs:

- *Oral administration*. We are developing our peptide therapeutics in a convenient capsule or tablet form intended for oral administration. We believe oral administration may reduce many of the problems and limitations associated with injections or infusions, including injection site pain and local reactions, inconvenience and anxiety, high rates of immunogenicity and potential safety risks.
- *Potential for improved safety and tolerability compared to antibody drugs.*
    - *Oral and GI-restricted delivery minimizes systemic exposure in the blood.* Oral GI-restricted delivery results in lower drug levels in the blood that may provide the potential for an enhanced safety profile over antibody drugs.
    - *Peptides can be cleared more quickly from systemic circulation.* Small molecules and peptides below a size threshold can be rapidly cleared from blood circulation by kidney filtration and excretion. Rapid clearance may be beneficial especially if patients need to discontinue therapy. In contrast, antibody drugs, because of their long plasma half-life, may take months to clear from blood circulation leaving patients exposed to continued or increased safety risk.
    - *The likelihood of much lower immunogenicity of small stable peptides compared to antibody drugs reduces the risk of loss of response.* We believe that ADAs are less likely to be elicited against constrained peptides, due to their small size, lack of epitope density, resistance to proteolysis, oral tolerance, and minimal systemic absorption.
- *Potential for localized delivery to site of disease.* We believe oral dosing of GI-restricted peptides results in substantially higher drug concentrations in the diseased GI tissue compartment compared to injectable antibody drugs. This targeted delivery to the site of action may lead to more immediate and significant target engagement at the site of active disease in the GI tissue compartment.
- *Cost-effective and less complex manufacturing*. Because of their size and stability, we believe that our oral, GI-restricted peptide product candidates can be produced, stored and shipped in a more cost-effective manner than many antibody drugs.

In chronic GI diseases such as IBD, we believe that our oral, GI-restricted peptide product candidates may offer improved delivery, the potential for improved safety and tolerability, and cost efficiencies that may provide an overall benefit to patients, payers, and physicians.

Figure 2: Oral Peptides vs. Injectable Antibody Drugs as Targeted Therapy for IBD



Overview of Inflammatory Bowel Disease

Inflammatory bowel disease is a group of chronic autoimmune and inflammatory conditions of the colon and small intestine, consisting primarily of UC and CD, and characterized by abdominal pain, diarrhea, weight loss, fatigue and anemia. In UC, inflammation starts in the rectum and generally extends proximally in a continuous manner through the entire colon. In CD, the disease most commonly affects the small intestine and the proximal large intestine. Both UC and CD have periods of various intensity and severity, and when a patient is symptomatic, the disease is considered to be in an active or flare stage. Approximately 25% of UC cases occur in persons before the age of 20. Furthermore, pediatric IBD is considered an orphan indication.

Market Overview

According to the Crohn's & Colitis Foundation of America, there were an estimated 1.6 million IBD patients in the United States in 2013, an increase of approximately 200,000 patients since 2011. As many as 70,000 new cases of IBD are diagnosed in the United States each year. As of 2008, annual direct treatment costs for patients with IBD in the United States were estimated to exceed $6.3 billion, while indirect costs such as missed work days were estimated to cost an additional $5.5 billion. In 2012, GlobalData estimated that the UC market reached approximately $4.2 billion and the CD market reached approximately $3.2 billion, in each case across ten major markets: the United States, France, Germany, Italy, Spain, the United Kingdom, Japan, Canada, China, and India. According to Global Data estimates, these markets are expected to grow at a compound annual growth rate of approximately 3% to 5% over the ten years from 2012 to 2022.

History of IBD Treatments

Non-Targeted Therapies

Sulfasalazine was discovered as the first non-targeted therapy for treatment of UC. Non-targeted therapies continued to evolve, including the introduction of corticosteroids for treatment of moderate UC in the 1950s. Subsequently, the immunosuppressive drug mercaptopurine was identified for UC in the 1960s, azathiopurine was developed in the 1970s, followed by 5-aminosalicylic acid. While these oral, non-targeted broad-spectrum anti-inflammatory agents and non-specific immunomodulators continue to be part of the IBD treatment paradigm, especially in mild-to-moderate IBD, these drugs are often ineffective, and corticosteroid and oral immunosuppressive drugs may have significant and disabling adverse effects that limit their use.

TNF-α and α4β7 Integrin Targeted Antibody Drugs

Recent advances in molecular biology and genomics ushered in the development of the potent and highly targeted biologic drugs. TNF-α was identified as a cytokine, a protein involved in cell signaling, that plays an important role in the inflammatory processes associated with IBD. In developing therapies against TNF-α, small molecule antagonists that directly bind TNF-α and other PPI targets have yet to be discovered and approved as therapeutics for the treatment of IBD. Thus, monoclonal antibody drugs emerged as a new class of therapeutics that can inhibit TNF-α activiy. There are currently five TNF-α antibody drugs (Humira®, Remicade®, Cimzia®, Simponi® and Inflectra® (infliximab biosimilar)) approved for the treatment of UC and/or CD. In 2014, Entyvio®, an intravenously administered antibody that selectively targets the α4β7 integrin, was approved for the treatment of adult patients with moderate-to-severe UC or CD where one or more standard therapies have not resulted in an adequate response. Entyvio® sales were approximately $530 million in 2015 and are projected to peak at approximately $2 billion.

While antibody drugs have greatly improved the treatment of IBD, they generally serve as the last-line of treatment before surgery due to their potential for severe adverse effects, diminishing efficacy over time, inherent limitations as injectable-based therapies and high costs of therapy.

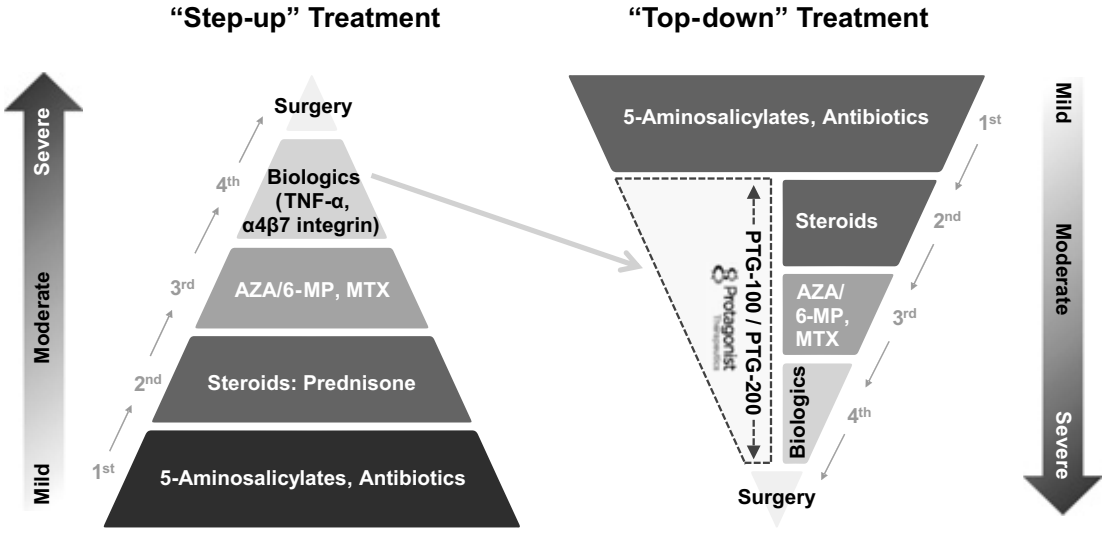
The Evolving IBD Treatment Paradigm

Inducing and maintaining clinical remission is the primary goal of treatment for IBD patients. The current treatment paradigm for IBD is considered a "step-up" approach. It involves a sequential "step-up" in treatment to more potent but higher risk therapies according to the level of severity of the patient's disease. Thus, targeted biologic therapies are generally reserved for patients with moderate-to-severe disease who have failed to respond to non-targeted oral therapies including 5-ASA agents, corticosteroids and non-specific immunomodulators.

For moderate-to-severe IBD patients, physicians prescribe TNF-α antibody drugs and Entyvio®, an antibody drug inhibiting α4β7 integrin, to induce and maintain clinical remission. Patients who are transitioned to these targeted antibody drugs may fail to respond to treatment or lose response to some or all of these agents over time and may ultimately require surgery. Approximately 50% to 73% of CD and 65% of UC patients fail to reach remission with TNF-α antibodies. Furthermore, 30% to 40% of UC patients and approximately 40% of CD patients treated with TNF-α antibody drugs stop responding to these agents over time (secondary non-responders) at a rate of approximately 10% to 13% per year. Of the CD patients who initially benefit from TNF-α antibody drugs, 25% to 40% of these patients develop intolerable or serious adverse events or lose their response within the first year of therapy. Currently, a common approach for IBD patients with lack of efficacy or loss of response to TNF-α antibody drugs is to switch such patients to other TNF-α antibody drugs. Although this is initially successful in 40% to 60% of patients, there remains a lack of treatment options for patients who lose responses to multiple TNF-α antibody drugs. Further, patient non-adherence with TNF-α antibody drugs in IBD has been reported to be between approximately 30% to 45% with greater need for hospitalization.

The development of new, potent and targeted therapies for IBD with oral delivery may potentially offer more effective treatment options for moderate-to-severe IBD patients, and for those with mild-to-moderate disease as well. Many clinicians are now advocating for an earlier introduction of oral targeted therapeutics for mild-to-moderate IBD, or a so-called "top-down" approach (see Figure 3 below) to reduce, replace or delay the use of corticosteroids and non-specific oral immunomodulators. We believe we are well-positioned to be leaders in this emerging paradigm shift from "step-up" to "top-down" therapy. Our oral, GI-restricted, and targeted peptide drugs work on the same specific targets as injectable antibody drugs, thereby offering potentially improved patient safety, compliance and convenience.

Figure 3: Transforming the Existing IBD Treatment Paradigm with Oral Targeted Therapy Drugs



PTG-100: AN ORAL α4β7 INTEGRIN ANTAGONIST

PTG-100 was discovered through our peptide technology platform and is being developed as a potential first-in-class oral, GI-restricted α4β7 integrin-specific antagonist initially for patients with moderate-to-severe UC.

Mechanism of Action

Integrins, such as α4β7, are transmembrane proteins that regulate cellular movement into extravascular tissue and play an important role in modulating the inflammatory reaction in the gut. The α4β7 integrin is expressed on the surface of T cells, immune cells that help defend against foreign and potentially harmful substances that enter the body. The development of UC is driven by the migration of α4β7 T cells into the GI tissue compartment and their subsequent activation within the GI tissue compartment. The entry of α4β7 T cells into the GI tissue compartment is facilitated by the PPI between the α4β7 integrin and its corresponding ligand, MAdCAM-1, which is primarily expressed in the GI tissue compartment. Hence, the binding of α4β7 to MAdCAM-1 can be categorized as a GI-specific interaction and has been identified as an IBD-specific targeted therapeutic approach. By blocking the binding of α4β7 integrin to MAdCAM-1, PTG-100 may prevent T cells from entering the GI tissue compartment, thereby reducing inflammation that leads to the clinical manifestations of UC.

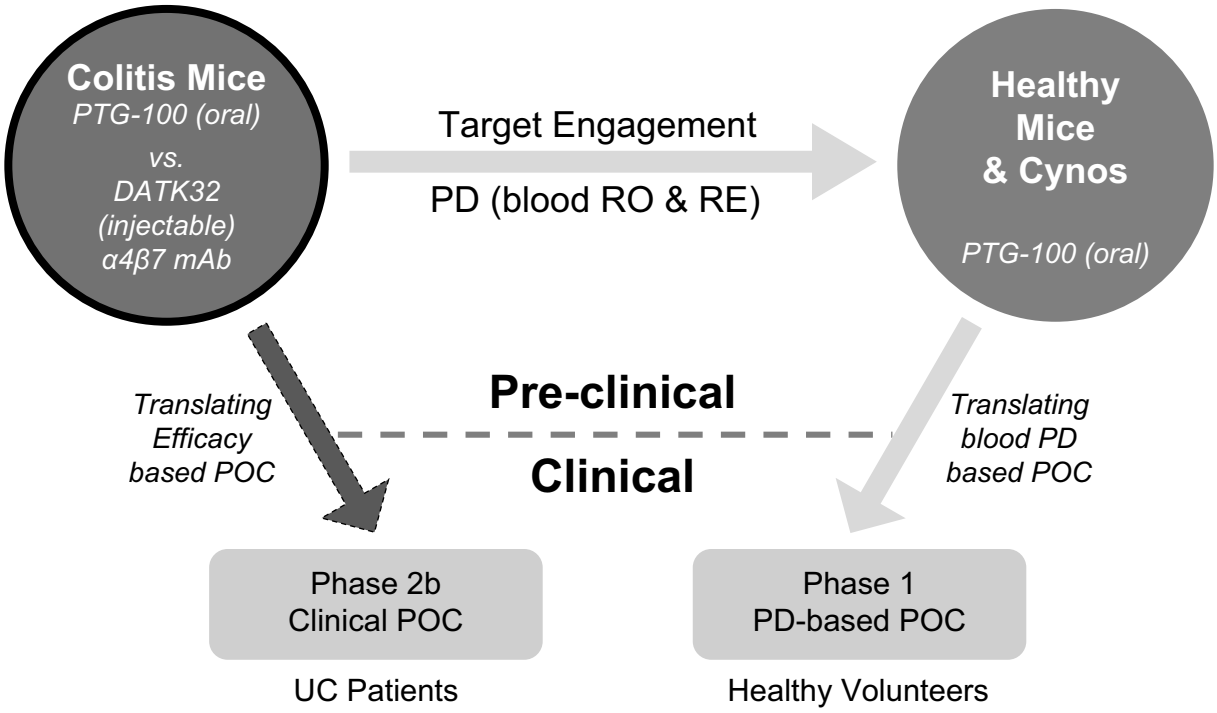
α4β7 for IBD is targeted by FDA-approved Entyvio® (vedolizumab), which has demonstrated safety and efficacy in patients with moderate-to-severe UC and CD. Since PTG-100 targets the same biological pathway as Entyvio®, we can utilize similar PD-based POC as early as in our pre-clinical studies and Phase 1 clinical trial to inform and guide our Phase 2b development program. We sourced these PD biomarker assays from public scientific publications and do not maintain any contractual arrangement providing access to this information with the makers of these marketed products.

Translating PTG-100's Pre-Clinical POC to Clinical POC

We have established a potentially efficacious dose range of PTG-100 in mice by demonstrating similar pharmacologic activity between oral PTG-100 and an injectable α4β7 antibody in mouse models of IBD. From this efficacious dose range in mice, approximately 6-50 mg/kg per day, we are able to directly estimate a potentially efficacious dose range in humans through allometric scaling based on whole body surface areas, which we determined to be approximately 33-300 mg per day.

Concurrently, we employed a complementary approach for establishing a potentially efficacious human dose range and early POC through specific blood PD response markers that reflect α4β7 integrin target engagement of PTG-100 in the GI tissue compartment and correlated those PD measurements with efficacy responses in mouse colitis models (Figure 4). Target engagement is a critical feature for demonstrating that PTG-100 can reach its intended target, thus inhibiting the trafficking of T cells into the GI tissue compartment. Our PD markers were monitored in mice and cynomolgus monkeys (cyno), which were similarly evaluated in normal healthy volunteers in our Phase 1 clinical trial. These blood PD responses have the potential to show that PTG-100 has engaged its intended α4β7 target in a manner that will help guide human dosing for our Phase 2b clinical trial.

Figure 4: Translating Pre-Clinical PK, PD and Efficacy Results to Human Clinical Trials



PTG-100's Pre-Clinical Proof-of-Concept Studies

Pre-clinical studies have demonstrated that PTG-100 is a potent and highly selective α4β7 antagonist with minimal systemic absorption. Mouse colitis models have further demonstrated that PTG-100 can inhibit T cell trafficking in the gut similar to the actions of the mouse α4β7 antagonist antibody.

PTG-100 potently inhibited binding of α4β7 to MAdCAM-1 in several human biochemical enzyme-linked immunosorbent assay (ELISA) and cell adhesion (transformed and primary cells) assays in a low nanomolar concentration range sufficient to inhibit 50% of binding (IC50) comparable to vedolizumab (Table 1). PTG-100 exhibited greater than a 100,000-fold selectivity against other structurally similar integrins, α4β1 and αLβ2, in cell adhesion assays which is comparable to the selectivity of vedolizumab (Table 1). PTG-100 was stable in *in vitro* assays simulating the GI tissue compartment, such as the small intestine and gastric stomach, with half-lives exceeding 12 hours (Table 1) and in human liver microsomes suggesting strong oral stability and the potential for once daily dosing in humans. PTG-100 did not affect the growth of and was not metabolized by common members of the human intestinal microflora. In total, these drug properties provide evidence to characterize PTG-100 as a potential first-in-class orally stable α4β7-specific antagonist. Furthermore, these drug properties allowed us to demonstrate proof-of-concept in animal colitis studies.

Table 1: PTG-100 *In Vitro* Potency, Selectivity, and Stability

	Potency (IC50, nM)			Integrin Selectivity (IC50, µM)		Stability ($T_{1/2}$), hrs	
	ELISA	Human Cell-based Assays					
	Human	Cell Line	Primary Blood	α4β1	αLβ2	Simulated Intestinal Fluid	Simulated Gastric Fluid
PTG-100	2	0.7	1.3	>100	>100	>12	>12

Non-clinical metabolism and PK studies demonstrated that much greater amounts of PTG-100 as measured by the maximum concentration (Cmax) as a percentage of total drug amount dosed orally, were present in the GI compartments, such as the small intestine, colon and feces compared to the systemic plasma and urine compartments of mice, rats, and cyno, thus confirming its GI-restricted properties (Table 2). Further, PTG-100 has an oral systemic bioavailability of less than 0.5%.

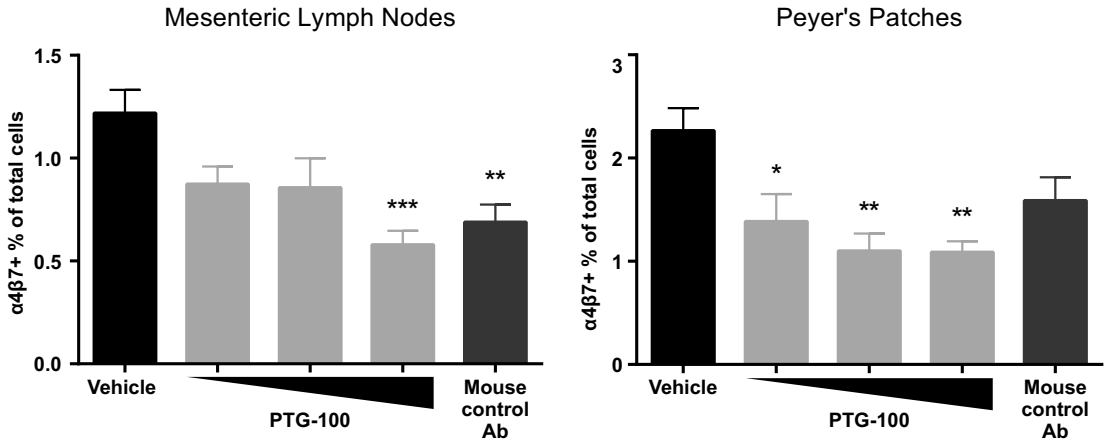
Table 2: PTG-100 Exposure in Plasma, GI, Urine and Feces

				Cmax (% of dose)			Cmax (% of dose)	
	Species	N	Dose (mg/kg)	Plasma	GI	Dose (mg/kg)	Urine	Feces
PTG-100	Mice	6	50	0.006	3.11	30	0.559	20.5
	Rat	3	50	0.046	13.56	10	0.064	27.6
	Cyno	3	10	0.021	nd(1)	10	0.291	14.6

(1) nd = not determined

We designed mouse colitis studies similar to those used for antibody drugs targeting this pathway to specifically monitor T cell trafficking to and from the GI tissue compartment (Figure 5). PTG-100 reduced α4β7 memory T cells migrating to the gut lymphoid tissues, including the mesenteric lymph nodes (MLN) and Peyer's patches (PP), under inflammatory conditions in the GI tissue compartment. Another example of the ability of PTG-100 to inhibit T cell trafficking was demonstrated by the reduction in the number of α4β7 cells in colon lesions in colitis mice. Furthermore, treatment benefit was demonstrated through blinded video endoscopy analysis for mucosal damage, and assessment of the incidence of bloody feces, which represent symptoms and measurements of UC in humans. In all studies in mouse models of colitis, the effects of oral PTG-100 were comparable to those of an injection of high doses of a positive control α4β7 antibody. This allows us to define the efficacious dose in mice with potential translation to the efficacious dose in humans.

Figure 5: PTG-100 Reduces Trafficking of Memory T Cells to MLN and Peyer's Patches



*** p≤0.05; ** p≤0.01; *** p≤0.001. A p-value is a measure of statistical significance of the observed result, or the probability that the observed result was achieved purely by chance. By convention, a p-value of 0.05 or lower is considered statistically significant (a p-value of <0.05 means that there is less than a 5% chance that the observed result was purely due to chance).**

Establishing Blood Pharmacodynamic Readouts of Target Engagement

We have used pre-clinical blood PD response markers that reflect target engagement in the GI tissue compartment and correlate with efficacy responses in mouse colitis studies to guide our dosing in human studies. Furthermore, we believe these pre-clinical blood PD responses, specifically receptor occupancy (RO) increases reflecting target engagement and receptor expression (RE) decreases reflecting subsequent pharmacologic activity, can be compared to the PD responses we observed in our Phase 1 clinical trial in healthy volunteers and ultimately can help to guide the dosing for evaluating clinical benefit in UC patients in the Phase 2b clinical trial. In the mouse colitis model, RO and RE were correlated with *in vivo* efficacy that can be extrapolated to the blood RO and RE observed in healthy mice and cyno. These PD markers from mice and cyno have specifically demonstrated increases in RO that peak at approximately 4 hours following a single dose (Table 3) and multiple doses (Figure 6A), and decreases in RE after multiple doses in healthy mice (Figure 6B) and colitis mice (Table 4). In translating the pre-clinical observations into a clinical setting, we are focused on evaluating dose- and time-dependent trends in RO and RE in our Phase 1 clinical trial that can be benchmarked to the animal data to give us greater confidence in progressing PTG-100 in clinical trials. Emphasis is placed on trends and not on absolute numbers owing to differences in GI transit times in different species and absence of absolute scaling methods from animals to humans for GI-restricted drugs.

Figure 6: (A) Percent Receptor Occupancy and (B) Receptor Expression of α4β7 on CD4+ Memory T Cells in Blood of Healthy Mice Dosed for 14 Days

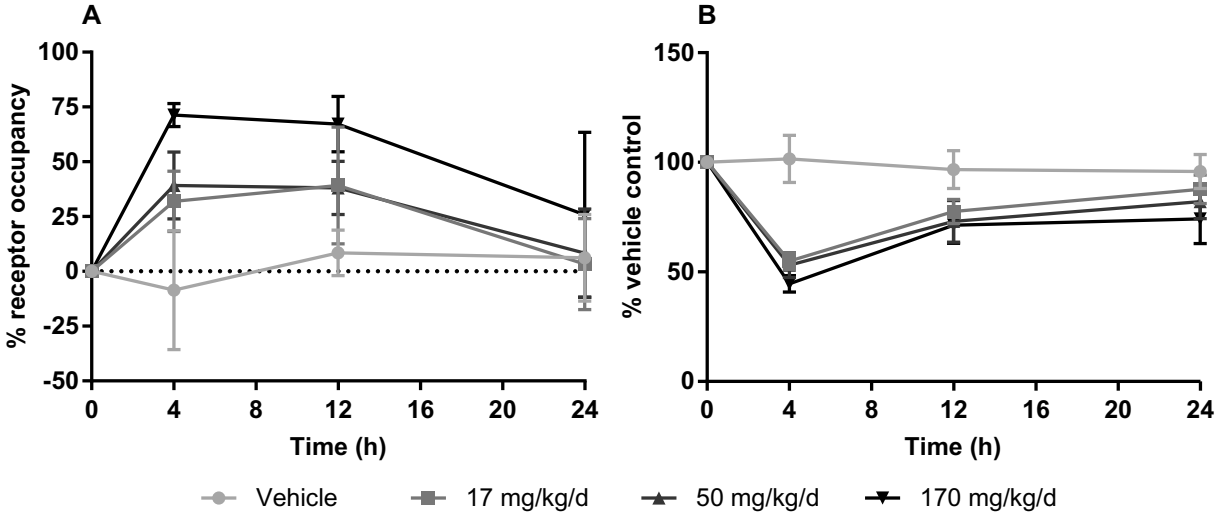


Table 3: PTG-100 Target Engagement—Receptor Occupancy in Healthy Cyno and Healthy Mice

Species	N	%RO 4 h post dose	%RO 24 h post dose
Cyno 12.5 mg/kg	3	76.2	27.6
Mice 50 mg/kg	4	90.1	nd

Table 4: PTG-100 Target Engagement—Receptor Expression in Colitis Mice and Healthy Cyno

Species	N	Dose (mg/kg)	%Target Expression Decrease after 7-14 Daily Doses
Mice	7	52.8	74.0
Cyno	4	12.5	33.7

PTG-100's Non-GLP and GLP Safety Pharmacology and Toxicology Studies

To date, all toxicology and safety pharmacology studies have not identified any safety issues. Good Laboratory Practices (GLP) toxicology studies in rats and cyno over 42 days of dosing showed that PTG-100 was well-tolerated at all dose levels with no dose-limiting toxicities. GLP are those procedural and operational requirements specified by FDA regulation to ensure the validity and reliability of nonclinical studies. No adverse effects were seen in either rat or cyno studies at all doses tested. Standard safety pharmacology and genotoxicity studies were similarly negative. We are currently conducting 12-week GLP toxicology studies to support the Phase 2b clinical trial.

PTG-100's Phase 1 Clinical Trial Overview

Following the submission and approval of a CTN, we initiated a Phase 1 randomized, double-blind, placebo-controlled clinical trial of PTG-100 in 78 normal healthy male volunteers in Australia, which was completed in June 2016. The Phase 1 SAD and MAD components were conducted with a solution-based liquid formulation of PTG-100. In the formulation bridging component of the trial, we compared the relative bioavailability of the liquid formulation to the capsule formulation that will be used in Phase 2b. In addition to determining the safety and tolerability and PK of PTG-100, the SAD and MAD components of the trial evaluated

PD-based POC through the assessment of α4β7 receptor occupancy that indicates target engagement and α4β7 target expression on peripheral blood memory T cells similar to what was done in the pre-clinical studies. These PD markers will also inform the estimation of dose range in the Phase 2b clinical trial.

Dosing of all planned cohorts has now been completed. The trial remains blinded to treatment assignment. We expect to have final unblinded data from the completed Phase 1 clinical trial by the end of the third quarter of 2016.

Safety and Tolerability

In both the SAD and MAD portions of the clinical trial, dose escalation proceeded from 100 mg up to the planned 1,000 mg dose level. There were no dose-limiting toxicities and the preliminary maximally tolerated dose has been established at 1,000 mg for both single and multiple dosing, the highest dose tested in the trial, although no dose-limiting toxicities were observed at the 1,000 mg dose level. There were no deaths or serious adverse events (SAEs) reported in the trial. All reported adverse events were of mild to moderate severity. There were no dose-dependent increases observed for any adverse events. The most frequent adverse events reported by subjects on PTG-100 were headache and upper respiratory tract infection. These events were also observed in subjects who took placebo.

Pharmacokinetics

PTG-100 plasma levels increased in a dose-dependent manner in both single and multiple dosing cohorts (Tables 5 and 6). Consistent with the pre-clinical data in mice, rats, and cyno, the blood levels of PTG-100 were extremely low as determined by the Area Under the Curve (AUC, which is a pharmacokinetic measurement of drug exposure in blood plasma against time) and Cmax (maximum concentration), thus demonstrating the GI-restricted nature of the drug. There was no apparent evidence of drug accumulation at Day 14 in the MAD cohorts perhaps related to the relatively short half-life (T1/2) in the blood (Tables 5 and 6).

Table 5: Pharmacokinetic Parameters of PTG-100 in the Phase 1 Clinical Trial SAD Component

PTG-100 (mg dose)	AUC (1) (h*ng/mL)	C_{max} % of Dose	$T_{1/2}$ Half Life (hours)
100	16.2	0.009%	3.85
300	47.0	0.007%	4.32
1,000	198	0.007%	5.80

Table 6: Pharmacokinetic Parameters of PTG-100 in the Phase 1 Clinical Trial MAD Component Human (Day 14)

PTG-100 (mg dose)	AUC (h*ng/mL)	C_{max} % of Dose	$T_{1/2}$ Half Life (hours)
100	9.44	0.006%	2.5
300	42.05	0.005%	5.7
1,000	145	0.003%	6.54

PTG-100 fecal levels increased in a dose-dependent manner in the multiple dosing cohorts. Minimum drug levels of PTG-100 were observed in urine samples, as expected, based on its characteristics as a GI-restricted drug with minimal systemic exposure (Table 7).

Table 7: PTG-100 Excretion in Urine and Feces in the Phase 1 Clinical Trial MAD Component Human (Day 14)

PTG-100 (mg dose)	% of Dose Excreted in Urine	% of Dose Excreted in Feces
300	0.118%	7.56%
1,000	0.067%	16.3%

Establishing Pharmacodynamic POC in Humans

Data from our mouse colitis studies support our conclusion that blood receptor occupancy is a correlate of target engagement in the GI tissue compartment in the dose ranges studied. In our Phase 1 clinical trial, blood receptor occupancy on CD4+ memory α4β7+ T cells increased in a dose-dependent and time-dependent manner (Figure 7A and Figure 8A). For receptor occupancy in the SAD cohorts (Figure 7A), treatment groups were significant compared to placebo at 100 mg ($p \leq 0.05$), 300 mg ($p \leq 0.005$) and 1,000 mg ($p \leq 0.0001$). In the MAD cohorts (Figure 8A), treatment groups were significant compared to placebo at 100 mg ($p < 0.0005$), 300 mg ($p < 0.0001$) and 1,000 mg ($p < 0.0001$) four hours post dose on Day 14.

An additional parameter of pharmacologic activity that we measured was the change in α4β7 expression on the blood memory T cells. Based on *in vitro* studies comparing vedolizumab and PTG-100, we expected that α4β7 expression would be reduced over time due to the internalization of the α4β7 receptor. Following single and multiple dose administration in the Phase 1 clinical trial, a dose-dependent and time-dependent reduction in α4β7 expression was observed, and it appears that the reduction in target expression may become saturated at 300 mg since a similar response was observed in the 1,000 mg cohort following both single and multiple dosing (Figure 7B and Figure 8B). For α4β7, downregulation of expression was significant in treatment groups, compared to placebo at 300 mg and 1,000 mg ($p \leq 0.01$).

The single dose 300 mg cohort was evaluated under fasted and fed (standard high fat diet) conditions. Blood drug levels and blood receptor occupancy of PTG-100 were compared under both conditions. Based on data from this SAD component and previous pre-clinical studies, the MAD component of the clinical trial was conducted under fed conditions.

Figure 7: (A) Percent Receptor Occupancy and (B) Expression of α4β7 on CD4+ Memory T Cells of Subjects Dosed in the Phase 1 SAD Component

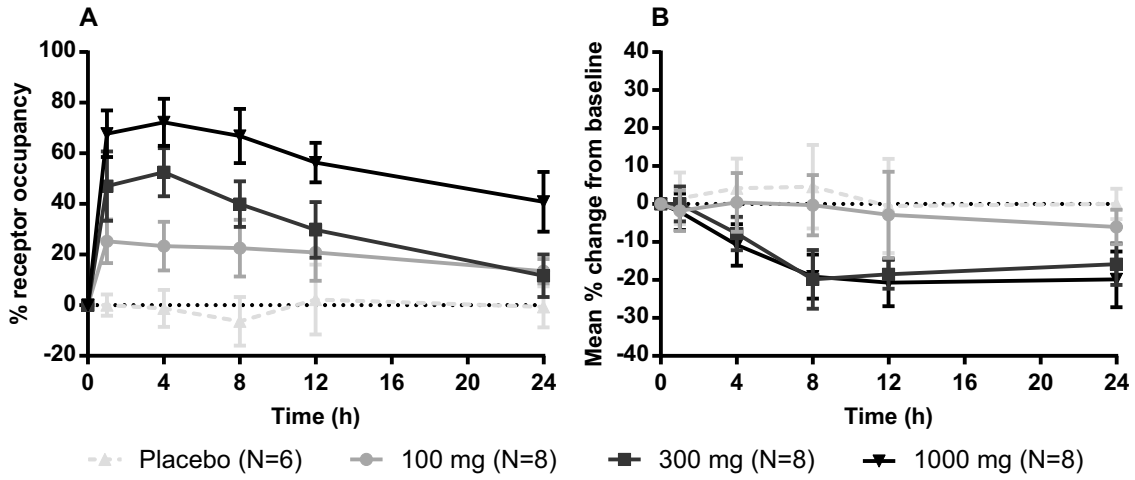
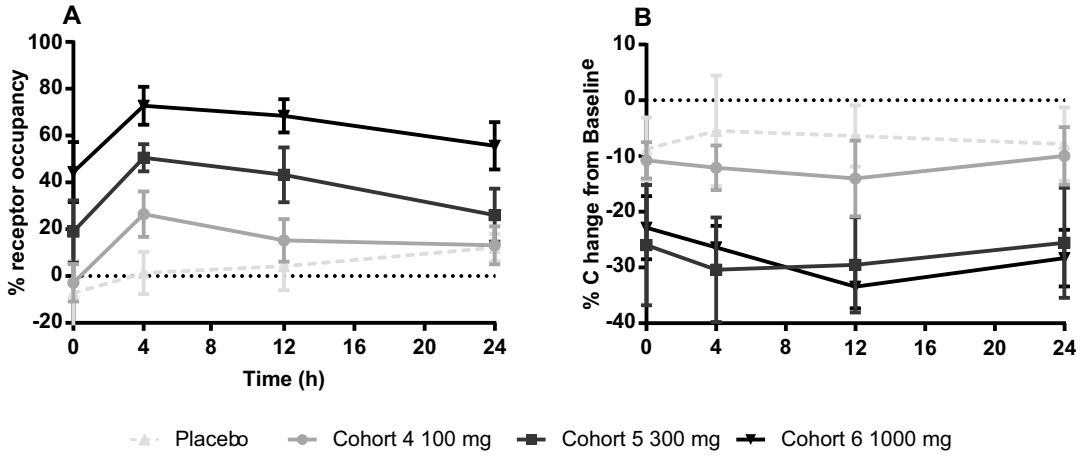


Figure 8: (A) Percent Receptor Occupancy and (B) Expression of α4β7 on CD4+ Memory T Cells of Subjects Dosed in the Phase 1 MAD Component at Day 14

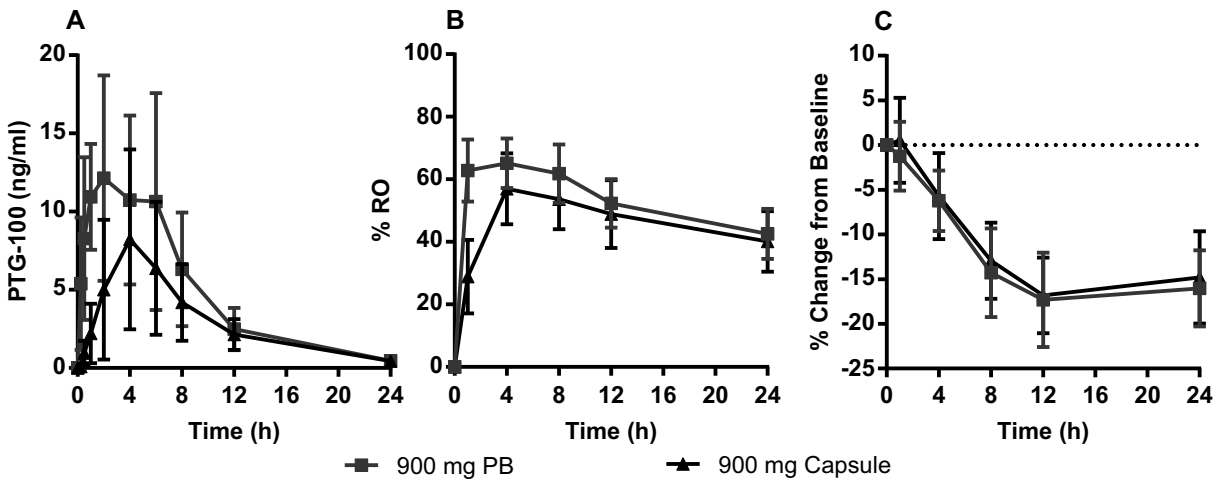


Thus, we observed dose-dependent and time-dependent target engagement and pharmacologic activity of PTG-100 following single- and multiple-dose administration in healthy volunteers consistent with observations in the animal studies.

Formulation Change from Phase 1 Clinical Trial to Phase 2b Clinical Trial

We utilized a liquid formulation in the SAD and MAD components of the Phase 1 clinical trial and we plan to introduce a capsule formulation of PTG-100 in the Phase 2b trial. To support this formulation change, we have completed an *in vivo* PK bridging study in cynos and have found the relative bioavailability in cynos of the capsule formulation comparable to the liquid formulation used in the Phase 1 clinical trial. In addition, we compared the PK in a single dose cross-over evaluation of the liquid and capsule formulation in normal healthy volunteers and observed that the plasma exposure of the capsule formulation was lower than that of the liquid formulation at the same dose level (Figure 9A). The PD effects were highly similar between the capsule and liquid formulations (RO/ Figure 9B and RE/Figure 9C), despite the lower plasma exposure of the capsule formulation. We believe this data will support the introduction of the capsule formulation in the Phase 2b clinical trial.

Figure 9: Formulation Bridging Component of Phase 1 (A) Plasma Drug Levels (B) Receptor Occupancy (C) Receptor Expression of α4β7 on CD4+ Memory T Cells in Blood



Planned Phase 2b Clinical Trial Design

Following U.S. IND submission, expected by the end of the third quarter of 2016, we plan to conduct a single global Phase 2b randomized, double-blind, placebo-controlled dose-finding clinical trial of PTG-100 in approximately 260 patients with moderate-to-severe UC. We plan to evaluate multiple dose levels of PTG-100 compared to placebo over 12 weeks in order to optimize induction dosing and duration of treatment prior to Phase 3 clinical trials. This plan incorporates FDA pre-IND meeting guidance into the design of the trial, which will be modeled after other recent Phase 2 studies of a wide range of antibody drugs developed and approved in patients with moderate-to-severe UC, including Entyvio®. We expect that this trial will support end-of-Phase 2 meetings with global health authorities and enable the initiation of a Phase 3 program.

The primary objectives of our Phase 2b clinical trial will be to evaluate the safety and tolerability and efficacy of PTG-100 in the induction of remission in subjects with moderate-to-severe UC. Secondary objectives are to select PTG-100 induction doses for continued development, to characterize PTG-100 plasma concentrations and to evaluate any potential immunogenicity over 12 weeks. The primary endpoint of the Phase 2b clinical trial will be the induction of clinical remission at 12 weeks. The trial will be statistically powered to detect a clinically meaningful difference in induction of remission in subjects with moderate-to-severe UC who are treated with PTG-100 compared to placebo. Secondary efficacy endpoints will include clinical response, endoscopic improvement, change in Mayo score, change in partial Mayo score, change in fecal calprotectin and change in the IBD questionnaire from baseline to be measured at multiple points during the induction period.

PTG-200: AN ORAL IL-23R ANTAGONIST

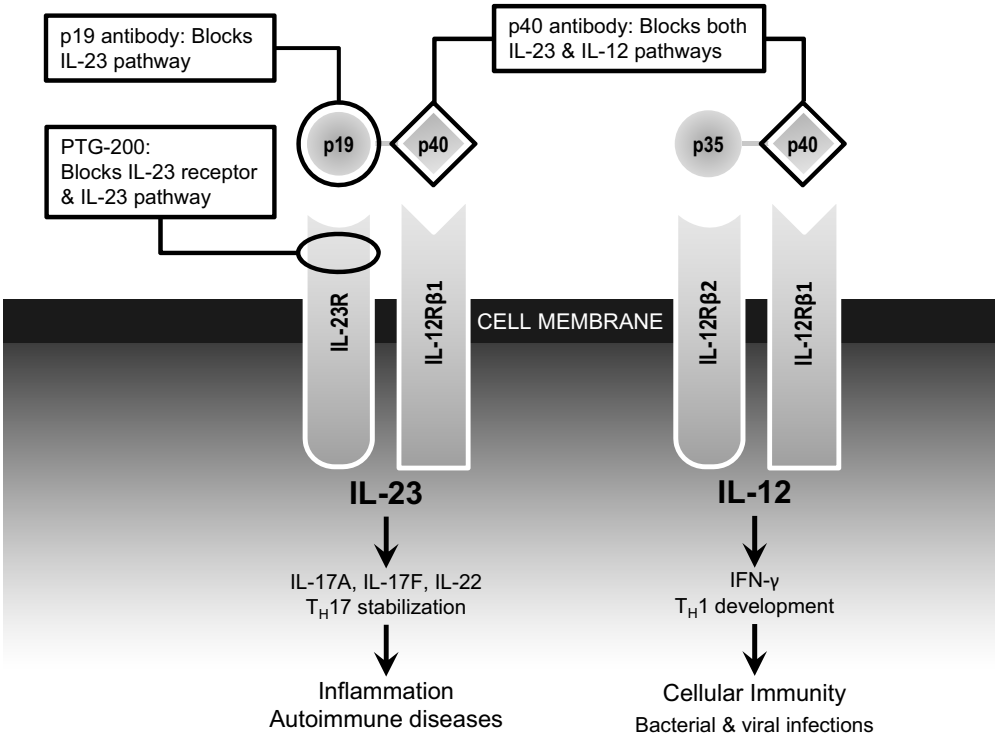
PTG-200 was discovered through our peptide technology platform and is being developed as a potential first-in-class oral, GI-restricted antagonist that binds to the specific subunit of IL-23R and blocks its interaction with the IL-23 cytokine. PTG-200 will be initially studied in patients with moderate-to-severe CD potentially followed by UC and pediatric IBD.

Mechanism of Action and Rationale

IL-23 is a member of the IL-12 family of cytokines with pro-inflammatory and autoimmune properties (Figure 10). Cytokines are cell signaling proteins that are released by cells and affect the behavior of other cells. Binding of the IL-23 ligand to the IL-23R leads to an expression of pro-inflammatory cytokines involved in the mucosal autocrine cascade that is an important pathway of many inflammatory diseases, including IBD. Furthermore, genetic analyses of IBD patients implicated IL-23R as a risk factor associated with susceptibility to IBD. The IL-23 pathway is targeted by the IL-12 and IL-23 antagonist infused antibody drug ustekinumab marketed as Stelara® for psoriasis and psoriatic arthritis. Stelara® has also recently reported positive Phase 3 data in moderate-to-severe CD. Next-generation IBD antibody drugs, such as guselkumab, target the p19 subunit of the IL-23 ligand to confer specificity for the IL-23 pathway that is believed to be an important driver of IBD pathology.

We believe that the oral, GI-restricted nature of PTG-200 will allow PTG-200 to be a potent inhibitor of IL-23R for the treatment of IBD. By targeting IL-23R with our GI-restricted oral IL-23R antagonist PTG-200, we believe PTG-200 will restore proper immune function in the GI tissue compartment where there is active disease while minimizing the risk of systemic side effects. Several key cell types that reside in gut-associated lymphoid tissue (GALT), including T cells, innate lymphoid cells, and natural killer cells, increase their expression of IL-23R during the progression of IBD. Therefore, the high concentrations of PTG-200 in GALT will facilitate access and binding to IL-23R expressed in the same tissue.

Figure 10: PTG-200—Specific Blockade of IL-23 Molecular Pathways



PTG-200's Pre-Clinical Proof-of-Concept Studies

PTG-200 potently inhibited binding of IL-23 to the IL-23 receptor in several biochemical (ELISA) and cell (transformed and primary) signaling assays in a subnanomolar to low nanomolar concentration range sufficient to inhibit 50% of binding (IC50, Table 8). PTG-200 exhibited greater than a 50,000-fold selectivity against other structurally similar receptors, IL-12Rβ1 and IL-6R (Table 8) thereby potentially reducing the risk of off target interactions. PTG-200 was stable in *in vitro* assays simulating the GI tissue compartment, such as the small intestine and gastric stomach, with half-lives exceeding 10 hours (Table 8) and in human liver microsomes suggesting strong oral stability and the potential for once daily dosing in humans. In total these drug properties provide evidence to characterize PTG-200 as a potential first-in-class potent and orally stable IL-23 receptor antagonist. Furthermore, these drug properties allowed us to demonstrate proof-of-concept in animal colitis studies.

Table 8: PTG-200 *In Vitro* Potency, Selectivity and Stability

Potency (IC50, nM)			Cytokine Receptor Selectivity (IC50, uM)		Stability (T1/2), hours	
ELISA	Human Cell-based Assays					
Human	Cell Line	Primary	IL-12Rβ1	IL-6R	Simulated Intestinal Fluid	Simulated Gastric Fluid
2	0.6	2.2	>100	>100	>12	>10

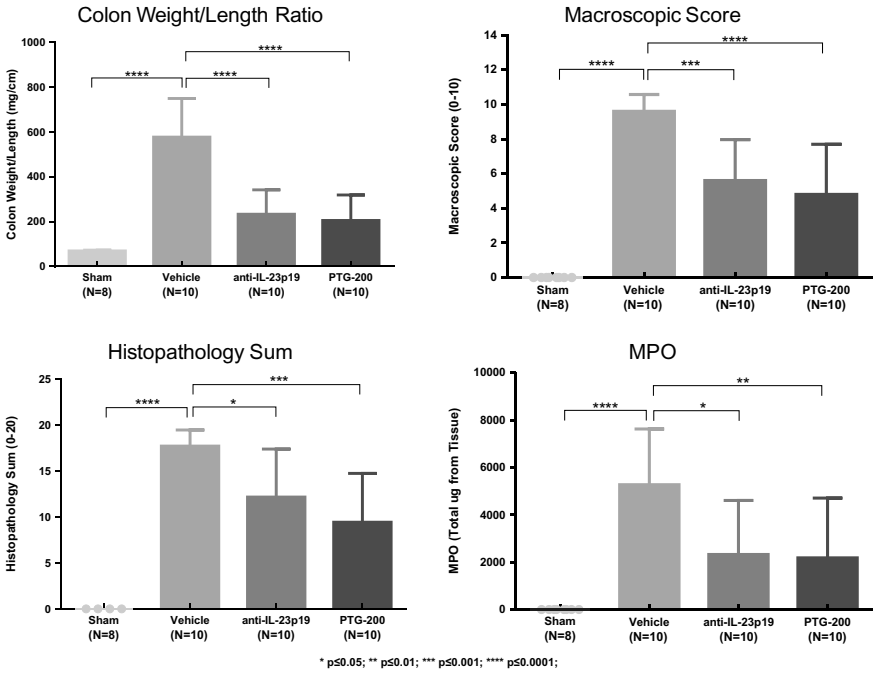
In PK studies in rats, PTG-200 was GI-restricted with less than 0.5% oral systemic bioavailability in plasma or urine and principal exposure in the small intestine, colon, and feces (Table 9). Very low oral bioavailability in cyno is also anticipated.

Table 9: PTG-200 Exposure in Plasma, GI, Urine and Feces

Species	N	Oral Dose (mg/kg)	Systemic Bioavailability %F	Cmax (% of dose)		CMax (% of dose)	
				Plasma	GI	Urine	Feces
Rat	3	10	0.00	0.000	0.830	0.000	7.68
Cyno	3	10	ND	0.001	ND	0.052	0.04

We have also completed pre-clinical POC studies in rat 2,4,6-trinitrobenzenesulfonic acid (TNBS) colitis models demonstrating that oral delivery of PTG-200 and other prototype antagonists significantly improved disease outcomes, such as reducing body weight loss, reducing the increased colon weight/length ratio, and reducing the increased colon macroscopic score which is comprised of assessments of colon adhesions, strictures, ulcers, and wall thickness (Figure 11). Furthermore, PTG-200 was found to reduce the increased histopathology summary score, which is comprised of assessments of mucosal and transmural inflammation, gland loss, and erosion parameters. Finally, PTG-200 was able to reduce the expression of the disease biomarker, myeloperoxidase (MPO) and other pro-inflammatory cytokines (Figure 11). MPO is an exploratory biomarker of innate inflammation and an indicator of a leaky mucosal barrier similar to fecal calprotectin, both of which can be measured in a stool test in human trials.

Figure 11: PTG-200 Reduces Pathology in Rat TNBS-Induced Colitis



The efficacy of oral PTG-200 seen in this IBD model was comparable to that of a positive control antibody against the rat IL-23p19 subunit which was present in the systemic blood compartment. This allows us to define the efficacious dose range in rats (approximately 28-61 mg/kg per day) with potential translation to the efficacious dose in humans.

PTG-200's Preliminary Pre-Clinical Safety Studies

In preliminary non-GLP toxicity studies in rats, PTG-200 was well-tolerated with no adverse events at the highest dose level tested. Further toxicology studies will be conducted to support first-in-human dosing. We have initiated manufacturing and IND-enabling studies in support of starting a Phase 1 clinical trial in 2017.

Proposed Clinical Plans

We plan to complete IND-enabling studies and to initiate a Phase 1 SAD and MAD clinical trial of PTG-200 in 2017 to evaluate safety, tolerability, and PK. Following completion of a Phase 1 clinical trial, we plan to initiate a randomized, double-blind, placebo-controlled Phase 2 POC clinical trial in patients with moderate-to-severe CD.

PTG-300: AN INJECTABLE HEPCIDIN MIMETIC

PTG-300 was discovered through our peptide technology platform and is being developed as a novel mimetic of hepcidin to potentially treat iron overload disorders such as transfusion-dependent β-Thalassemia, HH and SCD, each of which may qualify for orphan designation. Hepcidin is a naturally-occurring hormone involved in the transport and utilization of iron in the human body. Hepcidin has significant stability, potency, and solubility limitations. In order to effectively treat iron overload disorders in the body, we designed PTG-300 as a stable, soluble, hepcidin mimetic that can potentially be more potent and more amenable for weekly or less frequent subcutaneous delivery compared to hepcidin. We believe PTG-300 has the potential to improve disease symptoms and provide better safety by reducing the need for blood transfusions and chelator use in transfusion-dependent β-Thalassemia patients by treating both the underlying anemia and iron overload disorders. We have achieved POC in pre-clinical studies and have demonstrated that PTG-300 has the potential for greater potency, stability, and *in vivo* efficacy compared to natural hepcidin.

Mechanism of Action

The molecular target of hepcidin is the cellular trans-membrane protein ferroportin, which functions as an export channel for intracellular iron in macrophages, liver hepatocytes, and duodenal enterocytes. Upon binding to the extracellular domain of ferroportin, hepcidin decreases the delivery of iron to the blood circulation needed for the production of red blood cells.

Overview of β-Thalassemia and Current Therapies

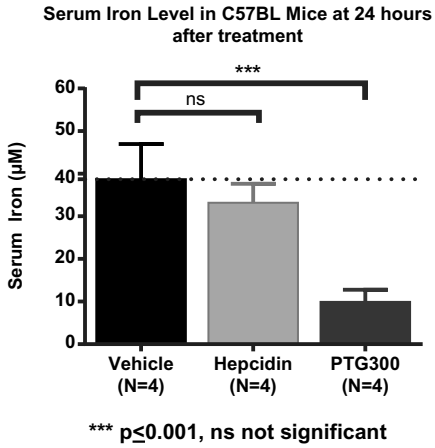
β-Thalassemia is potentially our first clinical indication for PTG-300. Patients with the most severe form of β-Thalassemia require chronic blood transfusions for survival, which results in additional serum iron release, exacerbating iron accumulation resulting in the need for chelators to treat the disease. A hepcidin mimetic will potentially be able to correct the anemia caused by the genetic mutation underlying β-Thalassemia, thus giving it a dual benefit of reducing the need for transfusion and reducing the excess circulating iron.

Globally, prevalence of β-Thalassemia is estimated to be approximately 200,000, with at least 60,000 patients born each year with the disease. In 2010, the β-Thalassemia market was estimated to be greater than $500 million, based largely on drugs consisting of chelating agents used to treat iron overload disorders arising from blood transfusions. The market is expected to grow to nearly $1 billion by 2018. β-Thalassemia has low prevalence in the Americas, with an estimated 2,750 patients and with approximately 300 patients born each year with the disease. Therefore, β-Thalassemia may qualify for FDA orphan designation.

PTG-300's Pre-clinical Proof-of-Concept Studies

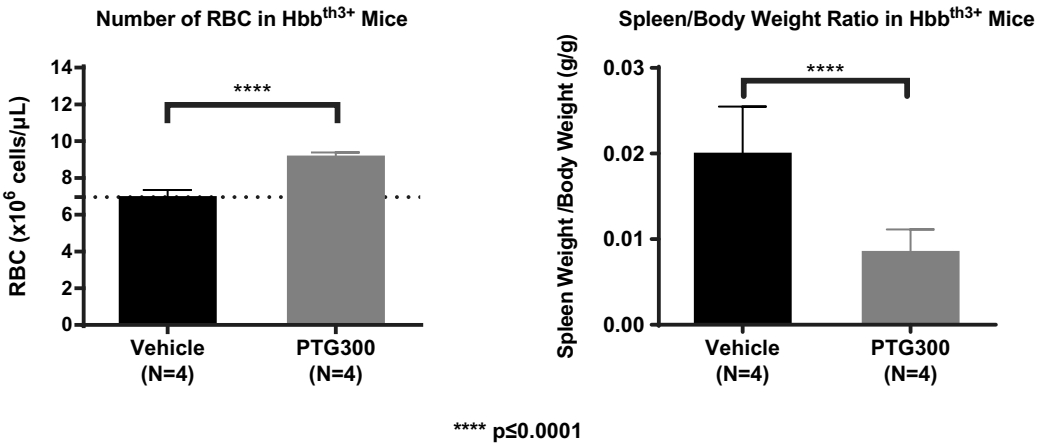
In pre-clinical studies, we demonstrated that PTG-300 can lower serum iron more effectively than hepcidin and maintain such lowered serum iron levels for at least 24 hours following a single subcutaneous injection (Figure 12).

Figure 12: PTG-300 is More Effective Than Hepcidin in Lowering Serum Iron in Healthy Mice



PTG-300 was also able to address the underlying anemia present in a mouse genetic model of β-Thalassemia, as shown by the significant increase in red blood cell number (RBC) and hemoglobin, and concomitant decrease in spleen weight, a reflection of compensatory splenomegaly (Figure 13).

Figure 13: PTG-300 Addresses Ineffective Erythropoiesis in Mouse β-Thalassemia



PTG-300's Pre-Clinical Development Program

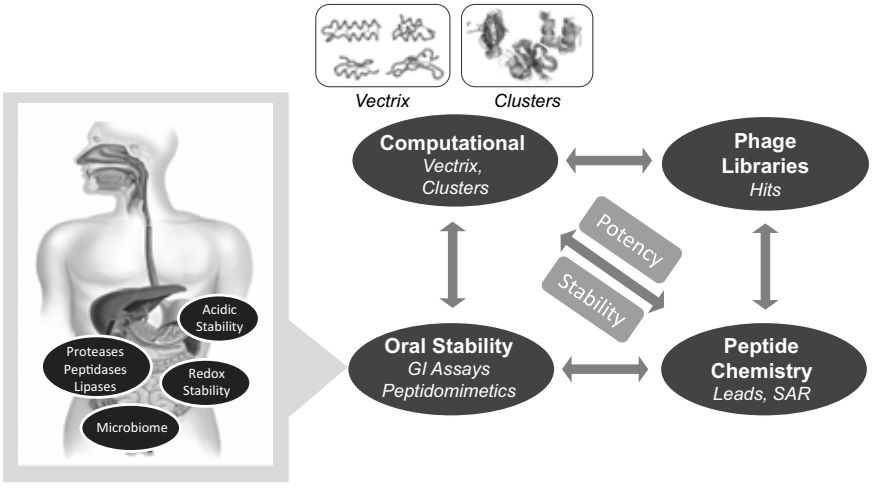
PTG-300 is being manufactured and formulated to support pre-clinical GLP toxicology and safety pharmacology studies, which will enable us to complete IND-enabling studies by the end of the first half of 2017. We expect to initiate a Phase 1 clinical trial in 2017.

OUR PEPTIDE TECHNOLOGY PLATFORM

Our proprietary technology platform has been successfully applied to a diverse set of biological targets that has led to several pre-clinical and clinical-stage peptide-based NCEs, including our only clinical-stage product candidate PTG-100, and our other product candidates in pre-clinical studies PTG-200 and PTG-300, for a variety of clinical indications. Our platform is comprised of a series of tools and methods, including a combination of molecular design, phage display, oral stability, medicinal chemistry, and *in vivo* pharmacology approaches (Figure 14).

The platform is used to develop potential drug candidates: (i) using the structure of a target, when available, (ii) when no target structure exists, or (iii) from publically disclosed peptide starting points. In a structure-based approach, our proprietary molecular design software and structural database of several thousand constrained peptides, termed Vectrix™, are screened to identify suitable scaffolds which form the basis of designing and constructing the first set of phage or chemical libraries. The initial hits are identified by either panning or screening such libraries, respectively. When structural information is unavailable for a target, hits are identified by panning a set of 34 proprietary cluster-based phage libraries consisting of millions of constrained peptides. Once the hits are identified, they are optimized using a set of peptide, peptide mimetic and medicinal chemistry techniques that include the incorporation of new or manipulation of existing cyclization-constraints, as well as natural or unnatural amino acids and chemical conjugation or acylation techniques. These techniques are applied to optimize potency, selectivity, stability, exposure and ultimately efficacy. For oral stability, a series of *in vitro* and *ex vivo* oral-stability assays that portray the chemical and metabolic barriers a peptide will encounter as it transits the GI tract are used to identify metabolically labile spots in the peptides. Such sites form the focus of medicinal-chemistry based optimization to engineer oral stability. Finally, various *in vivo* pharmacology tools are then used to quantify peptide exposure in relevant GI organs and tissues. The data can then be used to optimize required GI exposure and ultimately *in vivo* efficacy.

Figure 14: Our Peptide Technology Platform for Oral and Injectable Peptides



The key foundations of the platform include:

Molecular design tools and large database of constrained scaffolds

Through advances in genomics, molecular biology and structural genomic initiatives there has been an explosion in the number of known structures of potential new drug targets, including PPI targets. In particular, constrained peptides have the required surface complexity to match or complement the large flat surfaces of PPI targets to provide potent and selective drug candidates. We believe existing commercial molecular design software is not suitable, as it has been developed to identify small molecules that plug cavities of enzymes and do not bind to PPI targets.

We have developed a database of all known structures of a sub-class of constrained peptides, known as disulfide-rich peptides (DRPs). We have collected approximately 4,500 DRP scaffolds that are found throughout nature, ranging from single cell organisms to humans. We have created a proprietary molecular design environment, called Vectrix™. A pattern matching algorithm within Vectrix™ allows the selection of an appropriately stable DRP scaffold using the structure of the target of interest. This molecular design process is used to identify constrained peptides as starting points for hit discovery, which are ultimately optimized into potent, selective peptides against targets which are not amenable to small molecule drug discovery.

Phage display techniques and cluster libraries

Phage display may be used to discover the original hit based on Vectrix™-derived scaffolds, optimize existing hits, or to identify hits against those targets in which no structural information exists. For the latter targets, a series of pre-existing phage libraries, termed cluster libraries, are used for hit discovery. This includes 20 proprietary libraries of structurally diverse DRPs that sample greater than 85% of their known structural diversity and 14 proprietary libraries that sample different protein loop geometries. Collectively these libraries provide immense potential for discovering hits at diverse targets as they are based on natural-DRP scaffolds with these characteristics.

Oral stability and in vitro and ex vivo assays

The GI tract provides a set of chemical and metabolic barriers that hinder the development of oral therapeutic agents. We have developed numerous *in vitro* and *ex vivo* systems that profile peptide candidates for their stability features needed for oral delivery, GI restriction, and transit through the entire GI tract. This includes profiling for chemical stability, specifically pH and redox stability, and metabolic stability against proteases and other enzymes that are either of human or microbial origin.

These *in vitro* assays identify metabolic weak spots of peptides, which can then be stabilized by peptidic and peptidomimetic modifications without losing potency.

Medicinal peptide chemistry

We have significant expertise in optimizing potency, selectivity, oral stability and exposure of constrained peptides using a combination of peptide-cyclization, natural and unnatural amino acids, and various conjugation and acylation techniques. With respect to PTG-300, hit discovery and optimization relies exclusively on medicinal chemistry, with no phage display, to develop potent and selective injectable candidates with enhanced exposure in blood. For other targets, such as the discovery of PTG-100 and PTG-200, phage display is tightly coupled to medicinal chemistry and oral stability techniques to develop potent, selective and oral molecules that are GI-restricted.

In vivo pharmacology tools for GI restriction

When developing oral, GI-restricted constrained peptides, we correlate efficacy with potency and level of GI tissue compartment exposure. We have developed the required expertise and know-how to build PK and PD relationships to optimize physicochemical features of constrained peptides such that they are minimally absorbed and have the required degree of GI tissue compartment exposure over the required duration of time to achieve efficacy. This involves examining constrained peptide concentrations in various GI tissue compartments, blood, urine, and feces when delivered orally in rodents. In this fashion, we can understand the degree of tissue targeting, GI restriction and oral stability that is required to achieve efficacy.

Future Applications of our Platform

We believe we have built a versatile, well-validated and unique discovery platform. For example, this peptide technology platform has been used to develop product candidates at diverse target classes including G-protein-coupled receptors (GPCRs), ion channels, transporters and cytokines for a variety of therapeutic areas. In the future we may tackle other GI diseases and expand our delivery techniques to include other organ/tissue systems, such as the lung and eye, which will provide potential opportunities to pursue a variety of diseases. In addition, the gut may communicate with the immune, central nervous, and endocrine systems, providing the potential of our GI-restricted approach to treat metabolic, cancer and cardiovascular diseases. Lastly, we intend to progress our platform to achieve systemic bioavailability with peptides, thereby enabling us to address systemic diseases.

Material Agreements

Research Collaboration and License Agreement with Zealand Pharma A/S

In June 2012, we entered into a Research Collaboration and License Agreement with Zealand Pharma A/S (Zealand) to identify, optimize and develop novel DRPs to discover a hepcidin mimetic. Under the terms of the agreement, Zealand made an upfront payment and also funded the collaboration.

In October 2013, Zealand decided to abandon the collaboration program and, pursuant to the terms of the agreement, we elected to assume the responsibility for the development and commercialization of the product. Upon Zealand's abandonment, Zealand assigned to us certain intellectual property arising from the collaboration and also granted us an exclusive license to certain background intellectual property rights of Zealand that relate to the products assumed by us. Upon the nomination of PTG-300 as a development candidate, we owed Zealand a payment of $250,000. If we initiate a Phase 1 clinical trial for PTG-300, we will pay Zealand an additional $250,000. We have the right, but not the obligation, to further develop and commercialize the products and, if we successfully develop and commercialize PTG-300 without a partner, we will pay to Zealand up to an additional aggregate of $128.5 million for the achievement of certain development, regulatory and sales milestone events. In addition, we will pay to Zealand a low single digit royalty on worldwide net sales of the product until the later of ten years from the first commercial sale of the product or the expiration of the last patent covering the product. Due to Zealand's abandonment of the collaboration program and our assumption of the responsibility for the development and commercialization of the product, the agreement has terminated other than with respect to our potential milestone payments and royalty to Zealand.

Letter Agreement with Johnson & Johnson Development Corporation

In May 2013, in connection with our sale of Series B Stock, we entered into a letter agreement with JJDC, subsequently amended on April 19, 2016, pursuant to which we granted JJDC a right of first negotiation with respect to certain of our intellectual property rights, including PTG-200. For a full description of this agreement please see "*Certain Relationships and Related Person Transactions—Letter Agreement with Johnson & Johnson Development Corporation.*"

Competition

The biotechnology and pharmaceutical industries are characterized by continuing technological advancement and significant competition. While we believe that our product candidates, technology, knowledge and experience provide us with competitive advantages, we face competition from established and emerging pharmaceutical and biotechnology companies, academic institutions, governmental agencies and public and private research institutions, among others. There are no approved oral peptide-based $\alpha 4\beta 7$ integrins and IL-23 based product candidates for IBD.

In particular, we believe our principal competition in the treatment of IBD will come from companies with approved agents in the following therapeutic classes, among others:

- Infused $\alpha 4\beta 7$ antibody drugs: Takeda Pharmaceutical Company;
- Infused IL-23 and IL-12 antibody drug: Johnson & Johnson Services (Stelara® BLA filed for moderate-to-severe CD); and
- Injectable or infused TNF-α antibody drugs: Abbvie, Johnson & Johnson Services, Roche, UCB S.A.

We are also aware of several companies developing therapeutic product candidates for the treatment of IBD, including, but not limited to AstraZeneca, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene (mongersen sodium and ozanimod hydrochloride in Phase 3 clinical trials), Encycle Therapeutics, Genentech (etrolizumab in a Phase 3 clinical trial), Gilead Sciences (GS-5745 in a Phase 3 clinical trial), Pfizer (tofacitinib citrate in a Phase 3 clinical trial), and Roche.

We believe our principal competition in the treatment of iron overload disorders, such as β-Thalassemia, HH, and SCD, will come from other pipeline products being developed by companies such as Acceleron (luspatercept in a Phase 3 clinical trial), bluebird bio, Bristol-Myers Squibb, Emmaus Medical (glutamine in a Phase 3 clinical trial), Global Blood, La Jolla Pharmaceutical and Merganser, among others. We believe competition will also include approved iron chelation therapies that have been developed by Novartis and Apotex, among others.

Intellectual Property

We strive to protect and enhance the proprietary technology, inventions, and improvements that are commercially important to the development of our business, including seeking, maintaining, and defending patent rights, whether developed internally or licensed from third parties. We also rely on trade secrets relating to our proprietary technology platform and on know-how, and continuing technological innovation to develop, strengthen, and maintain our proprietary position in the field of peptide-based therapeutics that may be important for the development of our business. We will also take advantage of regulatory protection afforded through data exclusivity, market exclusivity and patent term extensions where available.

Our commercial success may depend in part on our ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to our business; defend and enforce our patents; preserve the confidentiality of our trade secrets; and operate without infringing the valid enforceable patents and proprietary rights of third parties. Our ability to stop third parties from making, using, selling, offering to sell or importing our products may depend on the extent to which we have rights under valid and enforceable patents or trade secrets that cover these activities. We cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our existing patents or any patents that may be granted to us in the future will be commercially useful in protecting our commercial products and methods of manufacturing the same. For more information, please see “Risk Factors—Risks Related to Our Intellectual Property.”

We have one issued patent and numerous patent applications related to our lead product candidates, and possess substantial know-how and trade secrets relating to the development and commercialization of peptide based therapeutic products. Our proprietary intellectual property, including patent and non-patent intellectual property, is generally directed to, for example, peptide-based therapeutic compositions, methods of using these peptide-based therapeutic compositions to treat or prevent disease, methods of manufacturing peptide-based therapeutic compositions, and other proprietary technologies and processes related to our lead product development candidates. As of the date of this prospectus, our patent portfolio includes the following:

- one issued patent and approximately 33 patents or patent applications that we exclusively own related to α4β7 integrin peptide antagonists;
- approximately 4 patent applications that we exclusively own related to IL-23R antagonist peptides;
- approximately 13 patent applications that we exclusively own related to hepcidin analogues; and
- other patent applications that we license or exclusively own related to our core technologies, including methods of peptide modification and characterization.

Our objective is to continue to expand our portfolio of patents and patent applications in order to protect our product candidates and related peptide-based drug technologies. Examples of the products and technology areas covered by our intellectual property portfolio are described below.

α4β7 Integrin Antagonist Peptides

The α4β7 integrin antagonist peptide patent portfolio includes one issued U.S. patent and pending patent applications directed to compositions of α4β7 integrin peptide monomers and dimers cyclized through intramolecular bonds and containing amino acid modifications conferring increased stability, potency and/or

selectivity, as well as methods of synthesizing and using these antagonist peptides to treat inflammatory disorders. Applications are currently pending in the United States and other major jurisdictions, including Australia, Canada, China, Japan, and Europe. Patent applications directed to PTG-100 composition of matter and uses thereof, if issued from the pending patent applications and if the appropriate maintenance, renewal, annuity or other governmental fees are paid, are expected to expire in October 2035 (worldwide, excluding possible patent term extensions). We expect other patent applications in this portfolio, if issued, and if the appropriate maintenance, renewal, annuity, or other governmental fees are paid, to result in patents that would expire from October 2033 to March 2037 (worldwide, excluding possible patent term extensions).

IL-23R Antagonist Peptides

The IL-23R antagonist peptide patent portfolio includes patent applications directed to compositions of IL-23R antagonist peptides cyclized through intramolecular bonds and containing amino acid modifications conferring increased stability, potency and/or selectivity, as well as methods of synthesizing and using these antagonist peptides to treat inflammatory disorders. Applications are currently pending in the United States and internationally. Patent applications directed to PTG-200 composition of matter and uses thereof, if issued from the pending patent applications and if the appropriate maintenance, renewal, annuity or other governmental fees are paid, are expected to expire in July 2035 (worldwide, excluding possible patent term extensions). We expect other patents and patent applications in this portfolio, if issued, and if the appropriate maintenance, renewal, annuity, or other governmental fees are paid, to expire from July 2035 to December 2036 (worldwide, excluding possible patent term extensions).

Hepcidin Mimetics Analogues

The hepcidin peptide analogues patent portfolio includes patent applications directed to compositions of hepcidin peptide analogues cyclized through intramolecular bonds and containing amino acid modifications conferring increased stability, potency and/or selectivity, as well as methods of synthesizing and using these hepcidin peptide analogues to treat iron-related disorders. Applications are currently pending in the United States and other major jurisdictions, including Australia, Canada, China, Japan, and Europe. Patent applications directed to PTG-300 composition of matter and uses thereof, if issued from the pending patent applications and if the appropriate maintenance, renewal, annuity or other governmental fees are paid, are expected to expire in March 2034 (worldwide, excluding possible patent term extensions). We expect other patents and patent applications in this portfolio, if issued, and if the appropriate maintenance, renewal, annuity, or other governmental fees are paid, to expire from March 2034 to December 2036 (worldwide, excluding possible patent term extensions).

Other

We also license patents and patent applications directed to processes and methods related to our technology platform. These patents have issued in the United States and other major jurisdictions, including Australia and Europe and are expected to expire between September 2019 and February 2023. Material aspects of our technology platform are protected by trade secrets and confidentiality agreements.

In addition to the above, we have established expertise and development capabilities focused in the areas of pre-clinical research and development, manufacturing and manufacturing process scale-up, quality control, quality assurance, regulatory affairs and clinical trial design and implementation. We believe that our focus and expertise will help us develop products based on our proprietary intellectual property.

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the date of filing the non-provisional application. In the United States, a patent's term may be lengthened by patent term adjustment, which compensates a patentee for administrative delays by the U.S. Patent and Trademark Office in granting a patent, or may be shortened if a patent is terminally disclaimed over an earlier-filed patent.

The term of a patent that covers an FDA approved drug may also be eligible for patent term extension, which permits patent term restoration of a U.S. patent as compensation for the patent term lost during the FDA regulatory review process. The Hatch-Waxman Act permits a patent term extension of up to five years beyond the expiration of the patent. The length of the patent term extension is related to the length of time the drug is under regulatory review. A patent term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only one patent applicable to an approved drug may be extended. Moreover, a patent can only be extended once, and thus, if a single patent is applicable to multiple products, it can only be extended based on one product. Similar provisions are available in Europe and other foreign jurisdictions to extend the term of a patent that covers an approved drug. When possible, depending upon the length of clinical trials and other factors involved in the filing of a new drug application (NDA), we expect to apply for patent term extensions for patents covering our product candidates and their methods of use.

Trade Secrets

We rely on trade secrets to protect certain aspects of our technology, particularly in relation to our technology platform. However, trade secrets can be difficult to protect. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our employees, consultants, scientific advisors and contractors. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our consultants, contractors or collaborators use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions. For more information, please see "Risk Factors—Risks Related to Our Intellectual Property."

Manufacturing

We contract with third parties for the manufacturing of all of our product candidates, including PTG-100, PTG-200, and PTG-300, for pre-clinical and clinical studies, and intend to continue to do so in the future. We do not own or operate any manufacturing facilities and we have no plans to build any owned clinical or commercial scale manufacturing capabilities. We believe that the use of contract manufacturing organization (CMOs) eliminates the need for us to directly invest in manufacturing facilities, equipment and additional staff. Although we rely on contract manufacturers, our personnel and consultants have extensive manufacturing experience overseeing CMOs. We regularly consider second source or back-up manufacturers for both active pharmaceutical ingredient and drug product manufacturing. To date, our third-party manufacturers have met the manufacturing requirements for the product candidates in a timely manner. We expect third-party manufacturers to be capable of providing sufficient quantities of our product candidates to meet anticipated full-scale commercial demands but we have not assessed these capabilities beyond the supply of clinical materials to date. We currently engage CMOs on a "fee for services" basis based on our current development plans. We plan to identify CMOs and enter into longer term contracts or commitments as we move our product candidates into Phase 3 clinical trials. We believe there are alternate sources of manufacturing that have been and could be engaged and enabled to satisfy its clinical and commercial requirements, however we cannot guarantee that identifying and establishing alternative relationships with such sources will be successful, cost effective, or completed on a timely basis without significant delay in the development or commercialization of our product candidates.

Government Regulation

The FDA and comparable regulatory authorities in state and local jurisdictions and in other countries impose substantial and burdensome requirements upon companies involved in the clinical development, manufacture, marketing and distribution of drugs, such as those we are developing. These agencies and other federal, state and local entities regulate, among other things, the research and development, testing, manufacture,

quality control, safety, effectiveness, labeling, storage, record keeping, approval, advertising and promotion, distribution, post-approval monitoring and reporting, sampling and export and import of our product candidates.

U.S. Government Regulation

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act (FDCA) and its implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with applicable federal, state, local and foreign statutes and regulations requires the expenditure of substantial time and financial resources. Failure to comply with the applicable U.S. requirements at any time during the product development process, approval process or after approval, may subject an applicant to a variety of administrative or judicial sanctions, such as the FDA's refusal to approve pending NDAs, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement or civil or criminal penalties.

The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- completion of pre-clinical laboratory tests, animal studies and formulation studies in compliance with the FDA's good laboratory practice (GLP) regulations;
- submission to the FDA of an IND application, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board (IRB) at each clinical site before each trial may be initiated;
- performance of adequate and well-controlled human clinical trials in accordance with good clinical practice (GCP) requirements to establish the safety and efficacy of the proposed drug product for each indication;
- submission to the FDA of an NDA;
- satisfactory completion of an FDA advisory committee review, if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with current good manufacturing practice (cGMP) requirements and to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity; and
- FDA review and approval of the NDA.

Pre-clinical Studies

Pre-clinical studies include laboratory evaluation of product chemistry, toxicity and formulation, as well as animal studies to assess potential safety and efficacy. An IND sponsor must submit the results of the pre-clinical tests, together with manufacturing information, analytical data and any available clinical data or literature, among other things, to the FDA as part of an IND. Some pre-clinical testing may continue even after the IND is submitted. An IND automatically becomes effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to one or more proposed clinical trials and places the clinical trial on a clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, submission of an IND may not result in the FDA allowing clinical trials to commence.

Clinical Trials

Clinical trials involve the administration of the investigational new drug to human subjects under the supervision of qualified investigators in accordance with GCP requirements, which include the requirement that all research subjects provide their informed consent in writing for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. A protocol for each clinical trial and any subsequent protocol amendments must be submitted to the FDA as part of the IND (or equivalent submission ex-US). In addition, an IRB or EC at each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution. Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health (NIH) for public dissemination on their www.clinicaltrials.gov website.

Human clinical trials are typically conducted in three sequential phases, which may overlap or be combined:

- Phase 1: The drug is initially introduced into healthy human subjects or patients with the target disease or condition and tested for safety, dosage tolerance, absorption, metabolism, distribution, excretion and, if possible, to gain an early indication of its effectiveness.
- Phase 2: The drug is administered to a limited patient population to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.
- Phase 3: The drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites, in well-controlled clinical trials to generate enough data to statistically evaluate the efficacy and safety of the product for approval, to establish the overall risk-benefit profile of the product, and to provide adequate information for the labeling of the product.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently if serious adverse events occur. Phase 1, Phase 2 and Phase 3 clinical trials may not be completed successfully within any specified period, or at all. Furthermore, the FDA or the sponsor may suspend or terminate a clinical trial at any time on various grounds, including a finding that the research subjects are being exposed to an unacceptable health risk. Similarly, an IRB or EC can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients.

Marketing Approval

Assuming successful completion of the required clinical testing, the results of the pre-clinical and clinical studies, together with detailed information relating to the product's chemistry, manufacture, controls and proposed labeling, among other things, are submitted to the FDA as part of an NDA requesting approval to market the product for one or more indications. In most cases, the submission of an NDA is subject to a substantial application user fee. Under the Prescription Drug User Fee Act (PDUFA) guidelines that are currently in effect, the FDA has a goal of ten months from the date of "filing" of a standard NDA for a new molecular entity to review and act on the submission. This review typically takes twelve months from the date the NDA is submitted to FDA because the FDA has approximately two months to make a "filing" decision.

In addition, under the Pediatric Research Equity Act of 2003 (PREA), as amended and reauthorized, certain NDAs or supplements to an NDA must contain data that are adequate to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations, and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements.

The FDA also may require submission of a risk evaluation and mitigation strategy (REMS), plan to ensure that the benefits of the drug outweigh its risks. The REMS plan could include medication guides, physician communication plans, assessment plans, and/or elements to assure safe use, such as restricted distribution methods, patient registries, or other risk minimization tools.

The FDA conducts a preliminary review of all NDAs within the first 60 days after submission, before accepting them for filing, to determine whether they are sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA reviews an NDA to determine, among other things, whether the drug is safe and effective and whether the facility in which it is manufactured, processed, packaged or held meets standards designed to assure the product's continued safety, quality and purity.

The FDA may refer an application for a novel drug to an advisory committee. An advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Before approving an NDA, the FDA typically will inspect the facility or facilities where the product is manufactured. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA may inspect one or more clinical trial sites to assure compliance with GCP requirements.

After evaluating the NDA and all related information, including the advisory committee recommendation, if any, and inspection reports regarding the manufacturing facilities and clinical trial sites, the FDA may issue an approval letter, or, in some cases, a complete response letter. A complete response letter generally contains a statement of specific conditions that must be met in order to secure final approval of the NDA and may require additional clinical or pre-clinical testing in order for FDA to reconsider the application. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when those conditions have been met to the FDA's satisfaction, the FDA will typically issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications.

Even if the FDA approves a product, it may limit the approved indications for use of the product, require that contraindications, warnings or precautions be included in the product labeling, require that post-approval studies, including Phase 4 clinical trials, be conducted to further assess a drug's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution and use restrictions or other risk management mechanisms under a REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-marketing studies or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Orphan Designation

The FDA may grant orphan designation to drugs or biologics intended to treat a rare disease or condition that affects fewer than 200,000 individuals in the United States, or if it affects more than 200,000 individuals in the United States, there is no reasonable expectation that the cost of developing and marketing the product for this type of disease or condition will be recovered from sales in the United States. Orphan designation must be requested before submitting a NDA or BLA. After the FDA grants orphan designation, the identity of the

therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

In the United States, orphan designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages and user-fee waivers. In addition, if a product receives the first FDA approval for the indication for which it has orphan designation, the product is entitled to orphan exclusivity, which means the FDA may not approve any other application to market the same product for the same indication for a period of seven years, except in limited circumstances, such as a showing of clinical superiority over the product with orphan exclusivity or where the manufacturer with orphan exclusivity is unable to assure sufficient quantities of the approved orphan designated product. Competitors, however, may receive approval of different products for the indication for which the orphan product has exclusivity or obtain approval for the same product but for a different indication for which the orphan product has exclusivity. Orphan product exclusivity also could block the approval of one of our products for seven years if a competitor obtains approval of the same biological product as defined by the FDA or if our product candidate is determined to be contained within the competitor's product for the same indication or disease. If a drug or biological product designated as an orphan product receives marketing approval for an indication broader than what is designated, it may not be entitled to orphan product exclusivity.

Post-Approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims are subject to prior FDA review and approval. There also are continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

The FDA may impose a number of post-approval requirements as a condition of approval of an NDA. For example, the FDA may require post-marketing testing, including Phase 4 clinical trials, and surveillance to further assess and monitor the product's safety and effectiveness after commercialization.

In addition, drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and state agencies, and are subject to periodic unannounced inspections by the FDA and these state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated and often require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP requirements and impose reporting and documentation requirements upon the sponsor and any third-party manufacturers that the sponsor may decide to use. Accordingly, manufacturers must continue to expend time, money, and effort in the area of production and quality control to maintain cGMP compliance.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in mandatory revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;

- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

Coverage and Reimbursement

Sales of our product candidates, if approved, will depend, in part, on the extent to which the cost of such products will be covered and adequately reimbursed by third-party payors, such as government healthcare programs, commercial insurance and managed health care organizations. These third-party payors are increasingly limiting coverage and/or reducing reimbursements for medical products and services by challenging the prices and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. If these third-party payors do not consider our products to be cost-effective compared to other therapies, they may not cover our products after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products on a profitable basis.

There is no uniform policy requirement for coverage and reimbursement for drug products exists among third-party payors in the United States. Therefore, coverage and reimbursement for drug products can differ significantly from payor to payor. The coverage determination process can be a time-consuming and costly process that may require us to provide scientific and clinical support for the use of our products to each payor separately, with no assurance that coverage and adequate reimbursement will be obtained or applied consistently. Even if reimbursement is provided, market acceptance of our products may be adversely affected if the amount of payment for our products proves to be unprofitable for health care providers or less profitable than alternative treatments, or if administrative burdens make our products less desirable to use.

In addition, the U.S. government, state legislatures and foreign governments have continued implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit our net revenue and results. Decreases in third-party reimbursement for our product candidates or a decision by a third-party payor to not cover our product candidates could reduce physician usage of our products candidates, once approved, and have a material adverse effect on our sales, results of operations and financial condition.

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, collectively referred to as the ACA, enacted in March 2010, has had and is expected to continue to have a significant impact on the health care industry. The ACA, among other things, imposes a significant annual fee on certain companies that manufacture or import branded prescription drug products. The ACA also increased the Medicaid rebate rate and expanded the rebate program to include Medicaid managed care organizations. It also contains substantial new provisions intended to broaden access to health insurance, reduce or constrain the growth of health care spending, enhance remedies against health care fraud and abuse, add new transparency requirements for the health care industry, impose new taxes and fees on pharmaceutical manufacturers, and impose additional health policy reforms, any or all of which may affect our business. Since its enactment, there have been judicial and Congressional challenges to certain aspects of the ACA, and there may be additional challenges and amendments to the ACA in the future. The ACA is likely to continue the downward pressure on pharmaceutical pricing, and may also increase our regulatory burdens and operating costs.

Other legislative changes have also been proposed and adopted since the ACA was enacted. For example, the Budget Control Act of 2011 resulted in aggregate reductions in Medicare payments to providers of 2% per fiscal year, which went into effect in 2013 and, following passage of the Bipartisan Budget Act of 2015, will stay in effect through 2025 unless additional Congressional action is taken. Additionally, the American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These new laws may result in additional reductions in Medicare and other health care funding.

It is uncertain whether and how future legislation, whether domestic or foreign, could affect prospects for our product candidates or what actions foreign, federal, state, or private payors for health care treatment and services may take in response to any such health care reform proposals or legislation. Adoption of price controls and other cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures reforms may prevent or limit our ability to generate revenue, attain profitability or commercialize our product candidates.

Other Health Care Laws and Compliance Requirements

We will also be subject to health care regulation and enforcement by the federal government and the states and foreign governments in which we will conduct our business once our products are approved. The laws that may affect our ability to operate include, but are not limited to: the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, which governs the conduct of certain electronic health care transactions and protects the security and privacy of protected health information. Criminal health care fraud statutes under HIPAA also prohibits persons and entities from knowingly and willfully executing a scheme to defraud any health care benefit program, including private payors, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for health care benefits, items or services; the federal health care programs' Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, in exchange for or to induce either the referral of an individual for, or the purchase, order or recommendation of, any good or service for which payment may be made under federal health care programs such as the Medicare and Medicaid programs; federal false claims laws and civil monetary penalties laws that prohibit, among other things, any person or entity from knowingly presenting, or causing to be presented, a false claim for payment to the federal government, or knowingly making, or causing to be made, a false statement to have a false claim paid; and the Physician Payments Sunshine Act, which requires certain manufacturers of drugs, devices, biologics, and medical supplies for which payment is available under Medicare, Medicaid, or Children's Health Insurance Program to report annually to the U.S. Department of Health and Human Services information related to payments and other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, and ownership and investment interests held by physicians and their immediate family members.

The majority of states also have statutes or regulations similar to the aforementioned federal anti-kickback and false claims laws, which apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor. We may be subject to state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts. In addition, we may be subject to reporting requirements under state transparency laws, as well as state laws that require pharmaceutical companies to comply with the industry's voluntary compliance guidelines and the applicable compliance guidance promulgated by the federal government that otherwise restricts certain payments that may be made to health care providers and entities.

Because of the breadth of these laws and the narrowness of available statutory and regulatory exceptions, it is possible that some of our business activities could be subject to challenge under one or more of such laws. If

we or our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, individual imprisonment, disgorgement, exclusion of products from reimbursement under U.S. federal or state health care programs, and the curtailment or restructuring of our operations.

Government Regulation Outside of the United States

In addition to regulations in the United States, we will be subject to a variety of regulations in other jurisdictions governing, among other things, clinical studies and any commercial sales and distribution of our products.

Whether or not we obtain FDA approval for a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical studies or marketing of the product in those countries. Certain countries outside of the United States have a similar process that requires the submission of a clinical study application much like the IND prior to the commencement of human clinical studies.

The requirements and process governing the conduct of clinical studies, product licensing, pricing and reimbursement vary from country to country. In all cases, the clinical studies are conducted in accordance with GCP and the applicable regulatory requirements and the ethical principles that have their origin in the Declaration of Helsinki.

If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

The requirements for conducting clinical trials in Australia, where we are currently conducting clinical trials for PTG-100, are as follows:

Conducting clinical trials for therapeutic drug candidates in Australia is subject to regulation by Australian governmental entities. Approval for inclusion in the Australian Register of Therapeutic Goods (ARTG) is required before a pharmaceutical drug product may be marketed in Australia.

Typically, the process of obtaining approval of a new therapeutic drug product for inclusion in the ARTG requires compilation of clinical trial data. Clinical trials conducted using “unapproved therapeutic goods” in Australia, being those which have not yet been evaluated by the Therapeutic Goods Administration (TGA) for quality, safety and efficacy must occur pursuant to either the Clinical Trial Notification (CTN) or Clinical Trial Exemption (CTX), process.

The CTN process broadly involves:

- completion of pre-clinical laboratory and animal testing;
- submission to a Human Research Ethics Committee (HREC) of all material relating to the proposed clinical trial, including the trial protocol. The TGA does not review any data relating to the clinical trial;
- final approval for the conduct of the clinical trial by the institution or organization at which the clinical trial will be conducted (Approving Authority), having due regard to the advice from the HREC; and
- notification of the clinical trial to the TGA.

The CTX process broadly involves:

- submission of an application to conduct a clinical trial to the TGA for evaluation and comment;
- a sponsor cannot commence a CTX trial until written advice has been received from the TGA regarding the application and approval for the conduct of the trial has been obtained from an ethics committee and the institution at which the trial will be conducted; and

- receipt of written advice from the TGA regarding the application.
- receipt of approval for the conduct of the trial from an ethics committee and the institution at which the trial will be conducted.

In each case, it is required that:

- adequate and well-controlled clinical trials demonstrate the quality, safety and efficacy of the therapeutic product;
- evidence is compiled which demonstrates that the manufacture of the therapeutic drug product complies with the principles of cGMP;
- manufacturing and clinical data is derived to submit to the Australian Committee on Prescription Medicines, which makes recommendations to the TGA as to whether or not to grant approval to include the therapeutic drug product in the ARTG; and
- an ultimate decision is made by the TGA whether to include the therapeutic drug product in the ARTG.

Pre-clinical studies include laboratory evaluation of the therapeutic drug product as well as animal studies to assess the potential safety and efficacy of the drug. The results of the pre-clinical studies form part of the materials submitted to the HREC in the case of a CTN trial and part of the application to the TGA in the case of a CTX trial.

Clinical trials involve administering the investigational product to healthy volunteers or patients under the supervision of a qualified principal investigator. The TGA has developed guidelines for a CTN. Under the CTN process, all material relating to the proposed trial is submitted directly to the HREC of each institution at which the trial is to be conducted. An HREC is an independent review committee set up under guidelines of the Australian National Health and Medical Research Council. The role of an HREC is to ensure the protection of rights, safety and wellbeing of human subjects involved in a clinical trial by, among other things, reviewing, approving and providing continuing review of trial protocols and amendments, and of the methods and material to be used in obtaining and documenting informed consent of the trial subjects. The TGA is formally notified by submission of a CTN application but does not review the safety of the drug or any aspect of the proposed clinical trial. The approving authority of each institution gives the final approval for the conduct of the clinical trial, having due regard to advice from the HREC. Following approval, responsibility for all aspects of the trial conducted under a CTN application remains with the HREC of each investigator's institution.

The standards for clinical research in Australia are set by the TGA and the National Health and Medical Research Council, and compliance with GCP is mandatory. Guidelines, such as those promulgated by the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use, or ICH, are required across all fields, including those related to pharmaceutical quality, nonclinical and clinical data requirements and study designs. The basic requirements for preclinical data to support a first-in-human study under ICH guidelines are applicable in Australia. Requirements related to adverse event reporting in Australia are similar to those required in other major jurisdictions.

Legal Proceedings

We are not currently a party to any material legal proceedings.

Facilities

As of June 30, 2016, we leased approximately 11,372 square feet of office and laboratory space in Milpitas, California, under a lease that expires in April 2018, with options to extend the lease for a period of three years. We believe that our existing facilities and arrangements are adequate to meet our business needs for at least the next 12 months and that additional space will be available on commercially reasonable terms, if required.

Employees

As of June 30, 2016, we had 29 full-time employees, 23 of whom were in research and development of which 2 hold an M.D. and 8 hold Ph.D. degrees. The remaining 6 employees worked in finance, business development, human resources and administrative support of which 2 hold a Ph.D. None of our employees is represented by a labor union or covered by a collective bargaining agreement. We consider our relationship with our employees to be good.

MANAGEMENT

Executive Officers and Directors

The following table sets forth the name, age and position of each of our executive officers, significant employees and directors as of July 1, 2016.

Name	Age	Position
Executive Officers		
Dinesh V. Patel, Ph.D.	59	President, Chief Executive Officer and Director
David Y. Liu, Ph.D.	66	Chief Scientific Officer and Head of Research & Development
Richard S. Shames, M.D.	56	Chief Medical Officer
Thomas P. O'Neil	51	Chief Financial Officer
William Hodder	52	Senior Vice President of Corporate Development
Significant Employees		
Ashok Bhandari, Ph.D.	52	Vice President of Chemistry
Larry Mattheakis, Ph.D.	59	Vice President of Biology
Mark Smythe, Ph.D.	51	Vice President of Technology & Alliances
Thamil Annamalai	56	Senior Director of Pre-clinical Development
Lucio Tozzi	52	Senior Director of Clinical Operations
Non-employee Directors		
Harold E. "Barry" Selick, Ph.D.	62	Chairman of the Board of Directors
Chaitan Khosla, Ph.D.	51	Director
Julie Papanek	33	Director
Armen B. Shanafelt, Ph.D.	57	Director
William D. Waddill[(1)]	59	Director

(1) Mr. Waddill was appointed to our board of directors effective as of July 1, 2016.

Executive Officers

Dinesh V. Patel, Ph.D.—Dr. Patel has served as a member of our board of directors and as our President and Chief Executive Officer since December 2008. Dr. Patel has more than 30 years of executive, entrepreneurial, and scientific experience spanning the pharmaceutical, biotechnology and biopharmaceutical industries. Prior to joining Protagonist, Dr. Patel served from 2006 to 2008 as the President and Chief Executive Officer of Arête Therapeutics, a privately held company focused on the development of drugs for metabolic syndrome. Prior to that, he was the President and Chief Executive Officer of Miikana Therapeutics, an oncology based company, from 2003 until it was acquired by Entremed (later renamed CASI Pharmaceuticals) in 2005. Prior to Miikana, Dr. Patel held positions of increasing responsibility at Versicor (later renamed Vicuron and which was acquired by Pfizer in 2015), from 1996 to 2003, most recently as Senior Vice President of Drug Discovery and Licensing. Prior to Vicuron, Dr. Patel was a director of chemistry at the combinatorial chemistry company Affymax, from 1993 to 1996. Dr. Patel was a medicinal chemist at Bristol-Myers Squibb from 1985 to 1993. Dr. Patel received his Ph.D. in Chemistry from Rutgers University, New Jersey and his B.S. in Industrial Chemistry from S. P. University, Vallabh Vidyanagar, India. We believe that because of his expertise, extensive knowledge of our Company and experience as an executive officer of biotechnology companies, Dr. Patel is able to make valuable contributions to our board of directors.

David Y. Liu, Ph.D.—Dr. Liu has served as our Chief Scientific Officer (CSO) since May 2013 and has served as CSO and Head of Research and Development since February 2016. Prior to Protagonist, Dr. Liu was the Chief Operating Officer and a co-founder of Trenovus, Inc., from 2010 to 2012. Prior to Trenovus, Dr. Liu was Vice President of Research at FibroGen Inc., from 2002 to 2010. Prior to Fibrogen, Dr. Liu served as Director of Inflammation Research at Scios, Inc., now part of Johnson & Johnson, from 1992 to 2002. Dr. Liu held a position as an academic researcher at Brigham and Women's Hospital, Harvard Medical School and was Instructor and Assistant Professor in the Department of Medicine, Harvard Medical School, from 1976 to 1986.

Dr. Liu received his Ph.D. in microbiology and immunology from Michigan State University, and his B.S. in chemistry from The University of Chicago.

Richard S. Shames, M.D.—Dr. Shames has served as our Chief Medical Officer since August 2015. He currently also serves as Adjunct Associate Clinical Professor of Pediatrics at Stanford University. Prior to joining Protagonist, he served as Senior Vice President and Chief Medical Officer at Aldea Pharmaceuticals, from 2013 to 2015. Prior to Aldea, Dr. Shames was Distinguished Scientist, Clinical Research and Early Biologics Lead (Immunology) at Merck & Co., Inc., from 2009 to 2013. Prior to joining Merck, Dr. Shames held positions of increasing responsibility at Facet Biotech (formerly PDL BioPharma), from 1999 to 2009, most recently as Therapeutic Head of Immunology and Senior Medical Director. Prior to Facet, Dr. Shames held full time clinical faculty positions in Pediatric Allergy and Clinical Immunology at Stanford University, from 1996 to 1999, and the University of California, San Francisco Schools of Medicine, from 1993 to 1996. Dr. Shames received his M.D. from University of California, Davis School of Medicine and received a B.S. in Biological Sciences from Stanford University.

Thomas P. O'Neil—Mr. O'Neil has served as our Chief Financial Officer since February 2016. From March 2015 to October 2015, Mr. O'Neil served as Chief Financial Officer of Arcadia Biosciences, Inc., a biopharmaceutical company. From January 2014 to July 2014, Mr. O'Neil served as Chief Financial Officer of Sorbent Therapeutics, Inc., a biopharmaceutical company. From September 2011 to December 2013, Mr. O'Neil served as a consultant to Sorbent and a variety of health care and technology companies. From December 2009 to August 2011, Mr. O'Neil served as Vice President of Finance & Administration of ChemGenex Pharmaceuticals Ltd., a biopharmaceutical company. From March 2007 to May 2009, Mr. O'Neil served as Vice President of Finance & Administration of Nodality, Inc., a biotechnology company. Mr. O'Neil holds a B.A. from Pomona College in International Relations and an M.B.A. from the University of California at Los Angeles.

William Hodder—Mr. Hodder has served as our Senior Vice President of Corporate Development since 2014. Prior to Protagonist, Mr. Hodder was Vice President, Business Development of Promedior, Inc. a clinical stage biotechnology company developing therapeutics for the treatment of fibrosis, from December 2013 to July 2014. Prior to joining Promedior, Mr. Hodder was a founder and CEO of start-up biotechnology company Trenovus, Inc., from 2010 to 2012. Previously, Mr. Hodder was Vice President of Business Development and Corporate Officer at FibroGen, Inc. Prior to joining FibroGen, he served a Director of Business Development and Marketing at Aradigm, a drug delivery company. Mr. Hodder received an M.B.A. from The University of Chicago Booth School of Business and received a B.S. in biology from Oakland University.

Significant Employees

Ashok Bhandari, Ph.D.—Dr. Bhandari joined Protagonist in 2011 and has served as our Vice President of Chemistry since February 2016. He has over 20 years of experience in the technology industry with expertise in peptide, medicinal, and combinatorial chemistry. Prior to joining Protagonist, Dr. Bhandari served as Associate Director of Chemistry at Affymax from 1994 to 2008. Dr. Bhandari has extensive experience with different peptide drug discovery and pre-clinical development programs on targets of protein-protein interactions. He received his Ph.D. in chemistry from Indian Institute of Chemical Technology, India and conducted post-doctoral research at University of California, Santa Barbara.

Larry Mattheakis, Ph.D.—Dr. Mattheakis joined Protagonist in 2012 and has served as our Vice President of Biology since 2016. Prior to joining Protagonist, Dr. Mattheakis served as the Associate Director at Exelixis, a publicly traded biotechnology company, from 2007 to 2011. Prior to Exelixis, he served as Senior Scientist at Cytokinetics from 2002 to 2007. Dr. Mattheakis began his career at Affymax Research Institute, where he served in a variety of roles, from 1992 to 2000, most recently as Research Fellow. Dr. Mattheakis received a Ph.D. in Biochemistry from the University of Wisconsin-Madison and a B.S. in Biochemistry from the University of California, Davis. He trained as a post-doctoral research fellow in the Department of Microbiology and Molecular Genetics at Harvard Medical School.

Mark Smythe, Ph.D.—Dr. Smythe is the founder of Protagonist and has served as our Vice President of Technology & Alliances since 2013, having previously served as our Chief Scientific Officer from 2009 to 2010 and our Chief Executive Officer from 2001 to 2009. He has extensive experience in industry-based research management and technology commercialization. Prior to Protagonist, he was Principal Investigator at the Centre for Drug Design and Development, now the Institute for Molecular Bioscience in Brisbane, Australia, from 1994 to 2001. Dr. Smythe earned a Ph.D. in Medicinal Chemistry from Melbourne University and a B.Sc (Hons) in Synthetic Organic Chemistry from James Cook University.

Thamil Annamalai—Ms. Annamalai has served as our Senior Director of Pre-clinical Development since March 2014. Ms. Annamalai has 25 years of research and development experience including more than a decade of drug discovery. From 2001 to 2013, Ms. Annamalai served as Manager, Director, and Senior Director for the *In Vivo* Evaluations group in Pre-clinical Development at Xenoport and was a member of the development team for its flagship product Horizant®. Ms. Annamalai was previously Manager of Pre-clinical Research at Intrabiotics Pharmaceuticals from 1997 to 2001, a biotechnology company focused on novel antimicrobial peptides. Prior to that, she was a Research Pharmacologist at Microcide pharmaceuticals from 1994 to 1997, Research Scientist at Nycomed Salutar from 1991 to 1994, and Toxicologist at Sola Barnes-Hind from 1989 to 1990. Ms. Annamalai received an M. Phil in Human Physiology from the Institute of Basic Medical Science, an M.Sc. in Zoology from Pachaiyappas College, and B.Sc. in Zoology from Stella Maris College, all institutions affiliated with University of Madras, India.

Lucio Tozzi—Mr. Tozzi has served as our Senior Director of Clinical Operations since July 2015. Mr. Tozzi has over 24 years of experience in global clinical trials spanning pharmaceuticals and medical devices in the therapeutic areas of infections, surgical morbidities, oncology, respiratory and CNS diseases. He has led clinical operations teams with responsibilities for clinical development, outsourcing, and project management. Prior to joining Protagonist, Mr. Tozzi was Senior Director and Head of Clinical Operations at Astex Pharmaceuticals, an oncology company (part of Otsuka), from August 2014 to July 2015. Prior to joining Astex, Mr. Tozzi was Director Clinical Operations at Baxter Healthcare from April 2005 to January 2014. Mr. Tozzi graduated with a BSc (Hons) in Biology from London University, Royal Holloway College, and holds a post-graduate Diploma (DipM) and Membership (MCIM) in Marketing from the Chartered Institute of Marketing.

Non-Employee Directors

Harold E. Selick, Ph.D.—Dr. Selick has served on our board of directors since February 2009. Dr. Selick has served as the Chief Executive Officer and a director of Threshold Pharmaceuticals, Inc. since June 2002. From June 2002 until July 2007, Dr. Selick was also a Venture Partner of Sofinnova Ventures, Inc., a venture capital firm. From January 1999 to April 2002, he was Chief Executive Officer of Camitro Corporation, a biotechnology company. From 1992 to 1999, he was at Affymax Research Institute, the drug discovery technology development center for Glaxo Wellcome plc, most recently as Vice President of Research. Prior to working at Affymax he held scientific positions at Protein Design Labs, Inc. and Anergen, Inc. Dr. Selick serves as Lead Director of PDL, a public company, and serves as Chairman of the board of directors of Catalyst Biosciences, a public company. Dr. Selick received his B.A. in Biophysics and Ph.D. in Biology from the University of Pennsylvania and was a Damon Runyon-Walter Winchell Cancer Fund Fellow and an American Cancer Society Senior Fellow at the University of California, San Francisco. We believe that because of his broad experience in building and running both private as well as public companies, combined with his experience serving on the boards of directors of a variety of biotechnology companies, Dr. Selick is well positioned to provide guidance and insight to the our board of directors and management team.

Chaitan Khosla, Ph.D.—Dr. Khosla has served as a member of our board of directors since October 2014. Dr. Khosla was the scientific founder and a member of the Board of Directors of Alvine Pharmaceuticals from 2005 until 2016. Prior to Alvine Pharmaceuticals, Dr. Khosla founded and was a director of Kosan Biosciences, from 1995 until it was acquired by Bristol-Myers Squibb in 2008. Dr. Khosla has been a Professor of Chemical

Engineering and Chemistry at Stanford University since 2001 and has been a faculty member since 1992. Since 2013, he has served as the founding Director of Stanford ChEM-H. Dr. Khosla is an elected member of the American Academy of Arts & Sciences and the National Academy of Engineering. He is the recipient of several awards, including the 1999 Alan T. Waterman award by the National Science Foundation, the 1999 Eli Lilly Award in biological chemistry and the 2000 ACS Award in pure chemistry. Dr. Khosla is the author of over 300 publications and is an inventor on numerous patents. Dr. Khosla received a Ph.D. from the California Institute of Technology. We believe that Dr. Khosla is qualified to serve on our board of directors because of his experience as a founder consultant and director of biotechnology companies and his expertise in the biotechnology field.

Julie Papanek—Ms. Papanek has served as a member of our board of directors since July 2015. Ms. Papanek has been a principal at Canaan Partners, a venture capital firm, since October 2014. Prior to Canaan, Ms. Papanek served in a variety of roles at Genentech across development and commercial, from March 2006 to June 2011. Ms. Papanek received an M.B.A. from the Stanford Graduate School of Business, an MPhil in BioScience Enterprise from Cambridge University, and a B.S. in Molecular Biophysics and Biochemistry from Yale University. We believe Ms. Papanek is qualified to serve on our board of directors because of her broad experience in finance and diverse expertise from across the entire medical spectrum.

Armen B. Shanafelt, Ph.D.—Dr. Shanafelt has served as a member of our board of directors since January 2010. Since April 2009, Dr. Shanafelt has been a partner of Lilly Ventures, a venture capital firm. Prior to joining Lilly Ventures, Dr. Shanafelt was Chief Science Officer responsible for the generation of the early biotherapeutic pipeline for Eli Lilly and Company, a pharmaceutical research company, spanning the therapeutic areas of oncology, endocrine, and neuroscience. Dr. Shanafelt currently serves as Chairman of the board of directors of Aeglea BioTherapeutics, Inc., a public biotechnology company, and serves as a director of the following privately held biotechnology companies: Aileron Therapeutics, Surface Oncology, Sutro Biopharma, and Symic Bio (Chairman). Dr. Shanafelt received his B.S. in Chemistry and Physics from Pacific Lutheran University, and his Ph.D. in Chemistry from the University of California, Berkeley. He completed his postdoctoral work at DNAX Research Institute, where he studied the structure-function relationships of cytokines and their receptors. We believe Dr. Shanafelt is qualified to serve on our board of directors because of his experience in the pharmaceutical, biotechnology and diagnostic businesses, including his expertise with respect to the generation of early biotherapeutic pipelines for oncology therapeutics.

William D. Waddill—Mr. Waddill has served as a member of our board of directors since July 2016. Since April 2014, Mr. Waddill has served as Senior Vice President, Chief Financial Officer, Treasurer and Secretary of Calithera Biosciences, Inc. From October 2007 to March 2014, Mr. Waddill served as Senior Vice President and Chief Financial Officer at OncoMed Pharmaceuticals, Inc., a biopharmaceutical company. From October 2006 to September 2007, Mr. Waddill served as the Senior Vice President, Chief Financial Officer of Ilypsa, Inc., a biotechnology company that was acquired in 2007 by Amgen, Inc. From February 2000 to September 2006, Mr. Waddill served as a Principal at Square One Finance, a financial consulting business. From December 1996 to February 2000, Mr. Waddill served as Senior Director of Finance and Administration at Exelixis, Inc., a biotechnology company. Mr. Waddill received a B.S. in Accounting from the University of Illinois, Chicago, and a certification as a public accountant, which is currently inactive, after working at PricewaterhouseCoopers LLP and Deloitte LLP. We believe that Mr. Waddill is qualified to serve on our board of directors because of his extensive experience in the biotechnology field.

Board Composition and Election of Directors

Certain members of our board of directors were elected pursuant to the provisions of our Voting Agreement, as amended. Under the Voting Agreement, as amended, our stockholders that are party to the Voting Agreement agreed to vote their shares to elect to our board of directors: (1) one individual who is the Chief Executive Officer (Dr. Patel); (2) one individual designated by the holders of a majority of the Series A Preferred Stock (Dr. Shanafelt); (3) one individual designated by the holders of a majority of the shares of Series B Preferred

Stock (currently vacant); (4) one individual designated by the holders of a majority of the shares of Series C Preferred Stock (Ms. Papanek); and (5) three individuals designated by the investors that hold a majority of the aggregate number of all shares of Common Stock as converted and the then outstanding shares of Series C Preferred Stock held by all investors (Dr. Selick, Dr. Khosla, and Mr. Waddill). The Voting Agreement will terminate upon the completion of this offering.

Director Independence

Our board of directors currently consists of six members. Our board of directors has determined that all of our directors, other than Dr. Patel, by virtue of his position as our Chief Executive Officer, are independent directors in accordance with the listing requirements of The NASDAQ Global Market. The NASDAQ independence definition includes a series of objective tests, including that the director is not, and has not been for at least three years, one of our employees and that neither the director nor any of his family members has engaged in various types of business dealings with us. In addition, as required by NASDAQ rules, our board of directors has made a subjective determination as to each independent director that no relationships exist, which, in the opinion of our board of directors, would interfere with the exercise of independent judgment in carrying out the responsibilities of a director. In making these determinations, our board of directors reviewed and discussed information provided by the directors and us with regard to each director's business and personal activities and relationships as they may relate to us and our management. There are no family relationships among any of our directors or executive officers.

Classified Board of Directors

In accordance with the terms of our amended and restated certificate of incorporation that will go into effect immediately prior to the completion of this offering, our board of directors will be divided into three classes with staggered, three-year terms. At each annual meeting of stockholders, the successors to directors whose terms then expire will be elected to serve from the time of election and qualification until the third annual meeting following election. Effective upon the completion of this offering, our directors will be divided among the three classes as follows:

- the Class I directors will be Julie Papanek and Dinesh V. Patel, Ph.D., and their terms will expire at our first annual meeting of stockholders following this offering;
- the Class II directors will be William D. Waddill and Chaitan Khosla, Ph.D., and their terms will expire at our second annual meeting of stockholders following this offering; and
- the Class III directors will be Armen B. Shanafelt, Ph.D. and Harold E. Selick, Ph.D., and their terms will expire at our third annual meeting of stockholders following this offering.

Our amended and restated certificate of incorporation that will go into effect immediately prior to the completion of this offering will provide that the authorized number of directors may be changed only by resolution of the board of directors. Any additional directorships resulting from an increase in the number of directors will be distributed among the three classes so that, as nearly as possible, each class will consist of one-third of the directors. The division of our board of directors into three classes with staggered three-year terms may delay or prevent a change of our management or a change in control of our company.

Board Leadership Structure

Our board of directors is currently led by its chairman, Dr. Harold Selick. Our board of directors recognizes that it is important to determine an optimal board leadership structure to ensure the independent oversight of management as the company continues to grow. We separate the roles of chief executive officer and chairman of the board in recognition of the differences between the two roles. The Chief Executive Officer is responsible for setting the strategic direction for the company and the day-to-day leadership and performance of the company,

while the chairman of the board of directors provides guidance to the Chief Executive Officer and presides over meetings of the full board of directors. We believe that this separation of responsibilities provides a balanced approach to managing the board of directors and overseeing the company.

Our board of directors has concluded that our current leadership structure is appropriate at this time. However, our board of directors will continue to periodically review our leadership structure and may make such changes in the future as it deems appropriate.

Role of Board in Risk Oversight Process

Our board of directors has responsibility for the oversight of the company's risk management processes and, either as a whole or through its committees, regularly discusses with management our major risk exposures, their potential impact on our business and the steps we take to manage them. The risk oversight process includes receiving regular reports from board committees and members of senior management to enable our board to understand the company's risk identification, risk management and risk mitigation strategies with respect to areas of potential material risk, including operations, finance, legal, regulatory, strategic, and reputational risk.

The audit committee reviews information regarding liquidity and operations, and oversees our management of financial risks. Periodically, the audit committee reviews our policies with respect to risk assessment, risk management, loss prevention, and regulatory compliance. Oversight by the audit committee includes direct communication with our external auditors, and discussions with management regarding significant risk exposures and the actions management has taken to limit, monitor or control such exposures. The compensation committee is responsible for assessing whether any of our compensation policies or programs has the potential to encourage excessive risk-taking. The nominating/corporate governance committee, will, immediately following the completion of this offering, manage risks associated with the independence of the board, corporate disclosure practices, and potential conflicts of interest. While each committee is responsible for evaluating certain risks and overseeing the management of such risks, the entire board is regularly informed through committee reports about such risks. Matters of significant strategic risk are considered by our board as a whole.

Board Committees and Independence

Our board has established an audit committee and a compensation committee, and effective immediately after the completion of this offering, a nominating and corporate governance committee—each of which operates or will operate under a charter that has been or will be approved by our board.

Audit Committee. The audit committee's main function is to oversee our accounting and financial reporting processes and the audits of our financial statements. This committee's responsibilities include, among other things:

- appointing our independent registered public accounting firm;
- evaluating the qualifications, independence and performance of our independent registered public accounting firm;
- approving the audit and non-audit services to be performed by our independent registered public accounting firm;
- reviewing the design, implementation, adequacy and effectiveness of our internal accounting controls and our critical accounting policies;
- discussing with management and the independent registered public accounting firm the results of our annual audit and the review of our quarterly unaudited financial statements;
- reviewing, overseeing and monitoring the integrity of our financial statements and our compliance with legal and regulatory requirements as they relate to financial statements or accounting matters;

- reviewing and approving any related party transactions; and
- reviewing and evaluating, at least annually, the performance of the audit committee and its members including compliance of the audit committee with its charter.

The members of our audit committee are William D. Waddill, Armen B. Shanafelt, Ph.D., and Julie Papanek. Mr. Waddill serves as the chairperson of the committee. All members of our audit committee meet the requirements for financial literacy under the applicable rules and regulations of the SEC and The NASDAQ Global Market. Our board of directors has determined that Mr. Waddill is an "audit committee financial expert" as defined by applicable SEC rules and has the requisite financial sophistication as defined under the applicable NASDAQ rules and regulations. Our board of directors has determined each of William D. Waddill, Armen B. Shanafelt, Ph.D., and Julie Papanek is independent under the applicable rules of the SEC and The NASDAQ Global Market. Upon the listing of our common stock on The NASDAQ Global Market, the audit committee will operate under a written charter that satisfies the applicable standards of the SEC and The NASDAQ Global Market.

Compensation Committee. The functions of our compensation committee include: (i) overseeing the compensation of our executive officers, (ii) administering our stock plans and make grants thereunder, (iii) overseeing our executive compensation policies, plans and programs generally, and (iv) recommending to the Board a set of corporate governance guidelines for us.

The members of our compensation committee are Harold E. Selick, Ph.D., William D. Waddill, and Julie Papanek. Dr. Selick serves as the chairperson of the committee. Our Board has determined that each of Harold E. Selick, Ph.D., William D. Waddill and Julie Papanek is independent under the applicable rules and regulations of The NASDAQ Global Market, is a "non-employee director" as defined in Rule 16b-3 promulgated under the Exchange Act and is an "outside director" as that term is defined in Section 162(m) of the Code, or Section 162(m). Upon the listing of our common stock on The NASDAQ Global Market, the compensation committee will operate under a written charter that will satisfy the applicable standards of the SEC and NASDAQ, which the compensation committee will review and evaluate at least annually.

Nominating and Corporate Governance Committee. The functions of the nominating and corporation governance committee will include: (i) reviewing periodically and evaluating director performance on our board of directors and its applicable committees, and recommending to our board of directors and management areas for improvement; (ii) interviewing, evaluating, nominating and recommending individuals for membership on our board of directors; (iii) reviewing and recommending to our board of directors any amendments to our corporate governance policies; and (iv) reviewing and assessing, at least annually, the performance of the nominating and corporate governance committee and the adequacy of its charter.

Effective immediately after this offering, the members of our nominating and corporate governance committee will be Armen B. Shanafelt, Ph.D., Harold E. Selick, Ph.D., and Chaitan Khosla, Ph.D. Dr. Shanafelt serves as the chairperson of the committee. Our Board has determined that each of Armen B. Shanafelt, Ph.D., Harold E. Selick, Ph.D., and Chaitan Khosla, Ph.D. is independent under the applicable rules and regulations of The NASDAQ Global Market and the SEC. Upon the listing of our common stock on The NASDAQ Global Market, the nominating and corporate governance committee will operate under a written charter that will satisfy the applicable standards of the SEC and NASDAQ, which the nominating and corporate governance committee will review and evaluate at least annually.

Compensation Committee Interlocks and Insider Participation

None of the members of the compensation committee is currently or has been at any time one of our officers or employees. None of our executive officers currently serves, or has served during the last year, as a member of the board of directors or compensation committee of any entity that has one or more executive officers serving as a member of our board of directors or compensation committee.

Code of Business Conduct and Ethics

We have adopted a written code of business conduct and ethics that applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. Upon the completion of this offering, our code of business conduct and ethics will be available under the Corporate Governance section of our website at www.protagonist-inc.com. In addition, we intend to post on our website all disclosures that are required by law or the listing standards of The NASDAQ Global Market concerning any amendments to, or waivers from, any provision of the code. The reference to our website address does not constitute incorporation by reference of the information contained at or available through our website, and you should not consider it to be a part of this prospectus.

Non-Employee Director Compensation

We have, from time to time, granted stock options to our non-employee directors. In October 2015, our board of directors granted Dr. Selick a nonstatutory stock option to purchase 155,510 shares of our common stock and Dr. Khosla a nonstatutory stock option to purchase 97,164 shares of our common stock under our 2007 Stock Option Plan. Dr. Selick's and Dr. Khosla's stock options were granted at an exercise price of $0.08 per share, and vests over four years, with 1/48 of the shares vesting on the last day of each month following September 1, 2015. Additionally, in June 2016, our board of directors approved the grant to Mr. Waddill of a nonstatutory stock option to purchase 188,144 shares of our common stock, such grant to become effective upon our board of directors' determination of the exercise price of Mr. Waddill's option. Mr. Waddill's nonstatutory stock option will vest over a period of two years, with 1/24 of the shares vesting on the last day of each month following July 1, 2016.

In October 2014, we entered into a service agreement with Dr. Khosla, pursuant to which Dr. Khosla began providing services to us as a member of our board of directors and as a member of our scientific advisory board. Under the terms of Dr. Khosla's service agreement, in consideration for his service as a member of our board of directors, Dr. Khosla is entitled to an annual fee in the amount of $25,000 that is paid in equal quarterly installments promptly following the conclusion of each calendar quarter, and in no event later than 15 days after the quarter in which the quarterly portion of the fee was earned. In order to receive the fee for a given quarter, Dr. Khosla must be serving as a director on the last day of the quarter, and his service agreement must remain in effect as of such day. In addition, under the terms of Dr. Khosla's service agreement, in consideration for his service as a member of our scientific advisory board, Dr. Khosla is entitled to an annual fee in the amount of $10,000 that is paid in equal quarterly installments promptly following the conclusion of each calendar quarter, and in no event later than 15 days after the quarter in which the quarterly portion of the fee was earned. In order to receive the fee for a given quarter, Dr. Khosla must be a member of our scientific advisory board on the last day of the quarter, and his service agreement must remain in effect as of such day.

In June 2013, our board of directors approved a compensation arrangement pursuant to which Dr. Selick would be paid for providing services to us as a member of our board of directors. Under the terms of such arrangement, Dr. Selick is entitled to an annual fee in the amount of $25,000 that is paid in equal quarterly installments promptly following the conclusion of each calendar quarter. In order to receive the fee for a given quarter, Mr. Selick must be serving as a director on the last day of the quarter.

In June 2016, our board of directors approved an annual cash retainer pursuant to which Mr. Waddill will be paid an annual fee of $25,000, payable quarterly, for providing services to us as a member of our board of directors.

We have reimbursed and will continue to reimburse all of our non-employee directors for their reasonable expenses incurred in attending meetings of our board of directors and committees of our board of directors.

The table below shows all compensation earned by or paid to our non-employee directors during the fiscal year that ended on December 31, 2015.

Name	Fees Earned or Paid in Cash ($)	Option Awards ($)(1)(2)	All Other Compensation ($)(3)	Total ($)
Harold E. Selick, Ph.D.	25,000	7,018	—	32,018
Chaitan Khosla, Ph.D.	25,000	4,386	10,000	39,386
Julie Papanek	—	—	—	—
Armen B. Shanafelt, Ph.D.	—	—	—	—
William D. Waddill	—	—	—	—

(1) The amounts in the "Option Awards" column reflect the aggregate grant date fair value of stock options granted during the calendar year computed in accordance with the provisions of Accounting Standards Codification (ASC) 718, *Compensation—Stock Compensation*. The assumptions that we used to calculate these amounts are discussed in the notes to our audited consolidated financial statements included elsewhere in this prospectus. These amounts do not reflect the actual economic value that will be realized by the named executive officer upon the vesting of the stock options, the exercise of the stock options, or the sale of the common stock underlying such stock options.

(2) The aggregate number of shares subject to each non-employee director's outstanding and unexercised option awards as of December 31, 2015 is set forth in the table below:

Name	Aggregate number of option awards outstanding as of December 31, 2015
Harold E. Selick, Ph.D.	26,720
Chaitan Khosla, Ph.D.	16,701
Julie Papanek	—
Armen B. Shanafelt, Ph.D.	—
William D. Waddill	—

(3) The amount in the "All Other Compensation" column represents consulting fees earned by or paid to Dr. Khosla during the fiscal year ended December 31, 2015.

Future Director Compensation

Following the consummation of this offering, we will implement a formal policy pursuant to which our non-employee directors will be eligible to receive compensation for service on our board of directors and committees of our board of directors.

EXECUTIVE COMPENSATION

Our named executive officers for the fiscal year ending on December 31, 2015, which consist of our principal executive officer and our two other most highly compensated executive officers, are:

- Dinesh V. Patel, Ph.D., our President and Chief Executive Officer;
- David Liu, Ph.D., our Chief Scientific Officer; and
- William Hodder, our Senior Vice President of Corporate Development.

2015 Summary Compensation Table

Name and Principal Position	Year	Salary ($)	Option Awards ($)(1)	Non-Equity Incentive Plan Compensation ($)(2)	Total ($)
Dinesh V. Patel, Ph.D.	2015	386,250	87,730	128,428	602,408
President and Chief Executive Officer					
David Liu, Ph.D.	2015	275,891	29,589	65,524	371,004
Chief Scientific Officer					
William Hodder	2015	242,388	36,150	58,594	337,132
Senior Vice President of Corporate Development					

(1) The amounts in the "Option Awards" column reflect the aggregate grant date fair value of stock options granted during the calendar year computed in accordance with the provisions of Accounting Standards Codification (ASC) 718, *Compensation—Stock Compensation*. The assumptions that we used to calculate these amounts are discussed in the notes to our audited consolidated financial statements included elsewhere in this prospectus. These amounts do not reflect the actual economic value that will be realized by the named executive officer upon the vesting of the stock options, the exercise of the stock options, or the sale of the common stock underlying such stock options.

(2) The amounts in the "Non-Equity Incentive Plan Compensation" column reflects cash bonuses earned for the 2015 fiscal year as determined by our board of directors based on the achievement of certain predetermined goals. For more information, see below under "—2015 Annual Bonus."

2015 Annual Base Salary

The base salary of our named executive officers is generally determined and approved at the beginning of each year or, if later, in connection with the commencement of employment of the executive, by our board of directors or the compensation committee. The following represent the 2015 annual base salaries for each of our named executive officers.

Name	2015 Base Salary ($)
Dinesh V. Patel, Ph.D.	386,250
David Liu, Ph.D.	275,891
William Hodder	250,000

2015 Annual Bonus

For the 2015 fiscal year, each of our named executive officers was eligible to earn an annual bonus up to a percentage of his annual salary, as set forth in the table below, based on the achievement of certain predetermined corporate and personal objectives as determined by our board of directors in its discretion. 100% of Dr. Patel's target bonus was contingent on the achievement of corporate objectives. 75% of Dr. Liu and Mr. Hodder's respective target bonus was contingent on the achievement of corporate objectives and 25% of Dr. Liu

and Mr. Hodder's respective target bonus was contingent on the achievement of individual objectives. Each named executive officer's objectives related to research and development, business development and finance, and the operation of the company. In February 2016, our board of directors determined the amount of each named executive officer's bonus based on the recommendations of our compensation committee. The amount of the bonus that each named executive officer earned for the fiscal year ending on December 31, 2015 is listed in the table below.

Name	Target Bonus	Amount of Bonus Earned
Dinesh V. Patel, Ph.D.	35%	$128,428
David Liu, Ph.D.	25%	$ 65,524
William Hodder	25%	$ 58,594

Equity-Based Incentive Awards

Our equity-based incentive awards are designed to align our interests and the interests of our stockholders with those of our employees, including our named executive officers. The board of directors is responsible for approving equity grants.

We have historically used stock options as the primary incentive for long-term compensation to our named executive officers because they are able to profit from stock options only if our stock price increases relative to the stock option's exercise price. We may grant equity awards at such times as our board of directors determines appropriate. Our executives generally are awarded an initial grant in the form of a stock option in connection with their commencement of employment. Additional grants may occur periodically in order to specifically incentivize executives with respect to achieving certain corporate goals or to reward executives for exceptional performance.

Prior to this offering, we have granted all stock options pursuant to our 2007 Stock Option and Incentive Plan (2007 Plan). Following this offering, we will grant equity incentive awards under the terms of our 2016 Equity Incentive Plan. The terms of our equity plans are described below under "—Equity Incentive Award Plans."

All options are granted with an exercise price per share that is no less than the fair market value of our common stock on the date of grant of each award. Our stock option awards generally vest over a four-year period and may be subject to acceleration of vesting and exercisability under certain termination and change of control events. Stock option awards granted under our 2007 Plan generally provide for accelerated vesting in the event of acquisition or a qualifying termination that occurs in connection with an acquisition.

For the fiscal year ending on December 31, 2015, we granted certain stock options to our named executive officers as described in the "Outstanding Equity Awards at 2015 Fiscal Year-End" table below.

Employment or Offer Letter Agreements with our Named Executive Officers

Below are written descriptions of our employment or offer letter agreements with each of our named executive officers. Each of our named executive officer's employment is "at will" and may be terminated at any time.

Employment Agreement with Dinesh V. Patel, Ph.D.

We entered into an employment agreement with Dinesh V. Patel. Ph.D., our President and Chief Executive Officer, in December 2008, which was subsequently amended in December 2015. The employment agreement provides for an initial base salary of $315,000, which has been subsequently increased a number of times, with the most recent increase to $400,000, effective as of January 1, 2016. The employment agreement also provides for an initial annual cash bonus of up to 30% of Dr. Patel's base salary, which has been subsequently increased a

number of times, with the most recent increase to 40% of Dr. Patel's base salary, effective as of January 1, 2016. The amount, if any, of such bonus with respect to any calendar year is based on the achievement of predetermined corporate and personal objectives as determined by our board of directors in its discretion.

Offer Letter Agreement with David Y. Liu, Ph.D.

We entered into an offer letter agreement with David Liu, Ph.D., our Chief Scientific Officer, in May 2013. The offer letter provides for an initial base salary of $250,000, which has been subsequently increased a number of times, with the most recent increase to $310,000, effective as of January 1, 2016. The offer letter also provides for an initial annual cash bonus of up to 25% of Dr. Liu's base salary, which was subsequently increased to 30% of Dr. Liu's base salary, effective as of January 1, 2016. The amount, if any, of such bonus with respect to any calendar year is based on the achievement of predetermined corporate and personal objectives as determined by our board of directors in its discretion.

Offer Letter Agreement with William Hodder

We entered into an offer letter agreement with William Hodder, our Senior Vice President of Corporate Development, in December 2014. The offer letter provides for an initial base salary of $250,000, which was subsequently increased to $260,000, effective as of January 1, 2016. The offer letter also provides for an initial annual cash bonus of up to 25% of Mr. Hodder's base salary. The amount, if any, of such bonus with respect to any calendar year is based on the achievement of predetermined corporate and personal objectives as determined by our board of directors in its discretion.

Potential Payments upon Termination or Change of Control

The Company is party to an Employee Severance Agreement with each of its named executive officers and certain of its other executives. If the Company terminates the employee's employment without "cause" or the employee terminates employment for "good reason" (each as defined in the agreement), the employee will receive: (a) salary continuation for 12 months, for our chief executive officer, or nine months, for our other named executive officers (18 months and 12 months, respectively, in the case of a change in control termination; (b) COBRA continuation for the salary continuation period (or an equivalent cash payment if required by law); (c) in the case of a change in control termination only, a monthly payment equal to one-twelfth of the target bonus for the severance period; and (d) in the case of a change in control termination only, acceleration of the vesting (and exercisability, if relevant) of equity awards held as of the date of termination. A "change in control termination" is a termination by the Company without "cause" or the employee for "good reason" that occurs within twelve months following the date of a "change in control," as defined in the agreement. Payments and benefits under the agreement are subject to the execution of an effective release.

Outstanding Equity Awards at 2015 Fiscal Year-End

The following table presents the outstanding equity incentive plan awards held by each named executive officer as of December 31, 2015.

		Option Awards			
Name	Grant Date	Number of Securities Underlying Unexercised Options Exercisable (#)	Number of Securities Underlying Unexercised Options Unexercisable (#)	Option Exercise Price ($)	Option Expiration Date
Dinesh V. Patel, Ph.D.	9/26/2013(1)	41,955	35,501	0.87	9/26/2023
	10/22/2014(1)	21,972	59,159	1.89	10/22/2024
	10/28/2015(2)	8,378	125,682	1.16	10/28/2025
David Y. Liu, Ph.D.	9/26/2013(1)	14,854	8,913	0.87	9/26/2023
	10/22/2014(1)	5,477	14,748	1.89	10/22/2024
	3/26/2015(2)	1,124	4,874	1.89	3/26/2025
	10/28/2015(2)	2,228	33,428	1.16	10/28/2025
William Hodder	3/26/2015(1)	—	25,995	1.89	3/26/2025
	10/28/2015(2)	—	14,087	1.16	10/28/2025

(1) 25% of the shares subject to the option vest on the first anniversary of the vesting commencement date, and the remainder vests in 36 equal monthly installments thereafter, subject to the holder continuing to provide services to us through the applicable vesting date. The option is subject to accelerated vesting in the event of an acquisition and in the event of a qualifying termination that occurs in the six months following the acquisition as described in "—Potential Payments upon Termination or Change of Control" above.

(2) The option vests as to 1/48 of the shares on the last day of each month following the vesting commencement date, subject to the holder continuing to provide services to us through the applicable vesting date. The option is subject to accelerated vesting in the event of an acquisition and in the event of a qualifying termination that occurs in the six months following the acquisition as described in "—Potential Payments upon Termination or Change of Control" above.

Equity Incentive Award Plans

2007 Stock Option and Incentive Plan

Our board of directors adopted our 2007 Plan in May 2007 and our stockholders approved our 2007 Plan in June 2007. Our 2007 Plan has been amended by our board of directors and our stockholders a number of times to increase the share reserve of the 2007 Plan, with the most recent amendment occurring in July 2015. Our 2007 Plan will terminate when our 2016 Plan becomes effective and no further stock awards will be granted under our 2007 Plan. As of March 31, 2016, there were a total of 783,341 stock options outstanding under our 2007 Plan.

Stock Awards. The 2007 Plan provides for the grant of incentive stock options, or ISOs, nonstatutory stock options, or NSOs, restricted stock awards, and other stock-based awards. ISOs may be granted only to our employees, including our named executive officers, and the employees of our affiliates. All other awards may be granted to our employees, including our named executive officers, our non-employee directors and consultants and the employees and consultants of our affiliates. No participant may be granted awards under the 2007 Plan to purchase more than 68,965 shares of our common stock during any one fiscal year unless waived in any instance by the board of directors. We have only granted stock options under the 2007 Plan.

Share Reserve. The aggregate number of shares of our common stock originally reserved for issuance pursuant to awards under the 2007 Plan was 80,329 shares. Pursuant to the most recent amendment to the 2007 Plan, an aggregate of 1,578,365 shares of our common stock were reserved for issuance pursuant to awards under the 2007 Plan. There will be no shares of our common stock available for issuance under the 2007 Plan when our 2016 Plan becomes effective. Outstanding awards under our 2007 Plan as of the effective date of our 2016 Plan

that expire or otherwise terminate without having been exercised in full and unvested shares issued pursuant to awards granted under the 2007 Plan that are forfeited to or repurchased by us will become available for grant under our 2016 Plan in accordance with its terms.

Administration. Our board of directors, or a duly authorized committee thereof, has the authority to administer the 2007 Plan. Subject to the terms of the 2007 Plan, our board of directors or the authorized committee, referred to here as the 2007 Plan administrator, determines the recipients, dates of grant, the numbers and types of stock awards to be granted and the terms and conditions of such stock awards.

The 2007 Plan administrator has the authority to amend, modify or terminate any outstanding award including, but not limited to, substituting therefor another award of the same or a different type, changing the date of exercise or realization, and converting an ISO to a NSO, provided that, the participant's consent to such action will be required unless the 2007 Plan administrator determines that the action, taking into account any related action, would not materially and adversely affect the participant.

Stock options. ISOs and NSOs are granted pursuant to stock option agreements adopted by the 2007 Plan administrator. The 2007 Plan administrator determines the exercise prices of stock options granted under the 2007 Plan. Stock options are exercisable at such times and subject to such terms and conditions as the 2007 Plan administrator specifies in the applicable option agreement.

Acceptable consideration for the purchase of common stock issued upon the exercise of a stock option are determined by the 2007 Plan administrator and may include (1) check payable to us, (2) a broker-assisted cashless exercise, (3) the tender of shares of our common stock previously owned by the participant, (4) delivery of a promissory note to us, and (5) other lawful consideration as determined by the 2007 Plan administrator.

Transferability. Unless the 2007 Plan administrator provides otherwise, awards generally are not transferable except by will and the laws of descent and distribution.

Changes to Capital Structure. In the event that there is a specified type of change in our capital structure, such as a stock split or recapitalization, appropriate adjustments will be made to the class and number of shares and exercise price or repurchase price per share of stock subject to all outstanding awards.

Acquisitions. In the event of certain specified a corporate transactions, in addition to any acceleration provisions expressly provided in the applicable option agreement, stock restriction agreement or any other agreement between a participant and us, upon consummation of an acquisition, the 2007 Plan administrator has the authority to accelerate the vesting of any stock awards. Upon consummation of an acquisition, the 2007 Plan administrator or the board of directors of the surviving or acquiring entity will make appropriate provision for the continuation of such awards by us or the assumption of such awards by the surviving or acquiring entity and by substituting on an equitable basis for the shares then subject to such awards either (a) the consideration payable with respect to the outstanding shares of common stock in connection with the acquisition, (b) the shares of stock of the surviving or acquiring corporation, or (c) such other securities as the 2007 Plan administrator deems appropriate, the fair market value of which will not materially differ from the fair market value of the shares of our common stock subject to such awards immediately preceding the acquisition. In addition to or in lieu of the foregoing, with respect to outstanding options, the 2007 Plan administrator may, upon written notice to the affected participants, provide that one or more options then outstanding will become immediately exercisable in full and that such options must be exercised within a specified number of days of the date of such notice, at the end of which period such options will terminate, or provide that one or more options then outstanding will become immediately exercisable in full and will be terminated in exchange for a cash payment equal to the excess of the fair market value for the shares subject to such options over the exercise price of such options.

Under the 2007 Plan, an "acquisition" is generally (1) any merger, consolidation or purchase of our outstanding capital after which our outstanding voting securities prior to such transaction represent (either by remaining outstanding or by being converted into or exchanged for voting securities of the surviving or acquiring

entity) less than 50% of the combined voting power of our voting securities or such surviving or acquiring entity outstanding voting securities immediately after such event, (2) any sale of all or substantially all of our assets or capital stock other than in a spin-off or similar transaction, or (3) any other acquisition of our business, as determined by the 2007 Plan administrator. However, an "acquisition" will not include any acquisition of our business where the consideration received or retained by the holders of our then outstanding capital stock does not consist primarily of (i) cash or cash equivalent consideration, (ii) securities which are registered under the Securities Act and/or (iii) securities for which we or any other issuer has agreed, including pursuant to a demand to file a registration statement within 90 days of completion of the transaction for resale to the public pursuant to the Securities Act.

Better After-Tax Provision. The 2007 Plan contains a "better after-tax" provision, which provides that if, in connection with an acquisition, any of the payments to a participant constitutes a parachute payment under Section 280G of the Code, then the number of awards that will become exercisable, realizable or vested in connection with such acquisition will reduced to the minimum extent necessary, so that no such tax would be imposed on the participant. However, if the aggregate present value of such awards would exceed the tax that would be imposed on the participant under Section 4999 of the Code, then such awards will continue to become exercisable, realizable or vested in connection with such acquisition

Amendment and Termination. The 2007 Plan administrator has the authority to amend, suspend, or terminate our 2007 Plan at any time. As discussed above, our 2007 Plan will terminate on the effective date of our 2016 Plan.

2016 Equity Incentive Plan

Our board of directors adopted our 2016 Equity Incentive Plan (2016 Plan) in July 2016 and our stockholders approved the 2016 Plan in July 2016 as the successor to our 2007 Plan. Our 2016 Plan will become effective upon the execution and delivery of the underwriting agreement related to this offering. No further stock awards will be granted under our 2007 Plan when the 2016 Plan becomes effective.

Stock Awards. The 2016 Plan provides for the grant of ISOs, NSOs, stock appreciation rights, restricted stock awards, restricted stock unit awards, performance based stock awards, and other stock awards, and performance cash awards. ISOs may be granted only to our employees, including our named executive officers, and the employees of our affiliates. All other awards and performance cash awards may be granted to our employees, including our named executive officers, our non-employee directors and consultants and the employees and consultants of our affiliates.

Share Reserve. Initially, the aggregate number of shares of our common stock that may be issued pursuant to stock awards under the 2016 Plan is the sum of (1) 1,200,000 shares, which includes the shares of our common stock reserved for issuance under our 2007 Plan at the time our 2016 Plan becomes effective, plus (2) any shares subject to outstanding stock options or other stock awards that were granted under our 2007 Plan that are forfeited, terminate, expire or are otherwise not issued. Additionally, the number of shares of our common stock reserved for issuance under the 2016 Plan will automatically increase on the first day of each fiscal year for ten years, beginning on the fiscal year following the fiscal year in which the 2016 Plan becomes effective, in an amount equal to 4% of the total number of shares of our capital stock outstanding on the last day of the preceding fiscal year, or a lesser number of shares determined by our board of directors.

If a stock award granted under the 2016 Plan expires or otherwise terminates without being exercised in full, or is settled in cash, the shares of our common stock not acquired pursuant to the stock award again will become available for subsequent issuance under the 2016 Plan. In addition, the following types of shares of our common stock under the 2016 Plan may become available for the grant of new stock awards under the 2016 Plan: (1) shares that are forfeited to or repurchased by us prior to becoming fully vested; (2) shares withheld to satisfy income or employment withholding taxes; or (3) shares used to pay the exercise or purchase price of a stock award. Shares issued under the 2016 Plan may be previously unissued shares or reacquired shares bought by us on the open market.

As of March 31, 2016, no awards have been granted under the 2016 Plan.

Incentive Stock Option Limit. The maximum number of shares of our common stock that may be issued upon the exercise of ISOs under the 2016 Plan is 3,500,000 shares.

Section 162(m) Limits. No person may be granted stock awards covering more than 1,000,000 shares of our common stock under the 2016 Plan during any fiscal year pursuant to stock options, stock appreciation rights and other stock awards whose value is determined by reference to an increase over an exercise or strike price of at least 100% of the fair market value on the date the stock award is granted. Additionally, no person may be granted in a fiscal year a performance stock award covering more than 1,000,000 shares of our common stock or a performance cash award having a maximum value in excess of $2,000,000. Subsequent stockholder approval of such limitations following the effectiveness of this offering will help to assure that any deductions to which we would otherwise be entitled with respect to such awards will not be subject to the $1,000,000 limitation on the income tax deductibility of compensation paid to any covered executive officer imposed by Section 162(m) of the Code.

Non-employee Director Limit. The maximum number of shares subject to awards granted during a single fiscal year to any non-employee director under the 2016 Plan, taken together with any cash fees paid to such nonemployee director during the fiscal year, will not exceed $500,000 in total value (calculating the value of any such awards based on the grant date fair value of such awards for financial reporting purposes). Our board of directors may make exceptions to this limit for individual non-employee directors in extraordinary circumstances (for example, to compensate such individual for interim service in the capacity of an officer of the Company), as our board of directors may determine in its discretion, provided that the non-employee director receiving such additional compensation may not participate in the decision to award such compensation or in other compensation decisions involving non-employee directors.

Administration. Our board of directors, or a duly authorized committee thereof, has the authority to administer the 2016 Plan. Our board of directors may also delegate to one or more of our officers the authority to (1) designate employees (other than other officers) to be recipients of certain stock awards, and (2) determine the number of shares of common stock to be subject to such stock awards. Subject to the terms of the 2016 Plan, our board of directors or the authorized committee, referred to here as the 2016 Plan administrator, determines recipients, dates of grant, the numbers and types of stock awards to be granted and the terms and conditions of the stock awards, including the period of their exercisability and vesting schedule applicable to a stock award. Subject to the limitations set forth below, the 2016 Plan administrator will also determine the exercise price or purchase price of awards granted and the types of consideration to be paid for the award.

Repricing; Cancellation and Re-Grant of Stock Awards. The 2016 Plan administrator has the authority to modify outstanding awards under the 2016 Plan. Subject to the terms of the 2016 Plan, the 2016 Plan administrator has the authority to reduce the exercise, purchase or strike price of any outstanding stock award, cancel any outstanding stock award in exchange for new stock awards, cash or other consideration, or take any other action that is treated as a repricing under generally accepted accounting principles, with the consent of any adversely affected participant.

Stock Options. ISOs and NSOs are granted pursuant to stock option agreements adopted by the 2016 Plan administrator. The 2016 Plan administrator determines the exercise price for a stock option, within the terms and conditions of the 2016 Plan, provided that the exercise price of a stock option generally cannot be less than 100% of the fair market value of our common stock on the date of grant. Options granted under the 2016 Plan vest at the rate specified by the 2016 Plan administrator.

The 2016 Plan administrator determines the term of stock options granted under the 2016 Plan, up to a maximum of ten years. Unless the terms of a participant's stock option agreement provide otherwise, if a participant's service relationship with us, or any of our affiliates, ceases for any reason other than disability, death or cause, the participant may generally exercise any vested options for a period of three months following

the cessation of service. The option term may be extended in the event that the exercise of the option following such a termination of service is prohibited by applicable securities laws or our insider trading policy. If a participant's service relationship with us or any of our affiliates ceases due to disability or death, or the participant dies within a certain period following cessation of service, the participant or a beneficiary may generally exercise any vested options for a period of 12 months in the event of disability and 18 months in the event of death. In the event of a termination for cause, options generally terminate immediately upon the termination of the individual for cause. In no event may an option be exercised beyond the expiration of its term.

Acceptable consideration for the purchase of common stock issued upon the exercise of a stock option will be determined by the 2016 Plan administrator and may include (1) cash, check, bank draft or money order, (2) a broker-assisted cashless exercise, (3) the tender of shares of our common stock previously owned by the participant, (4) a net exercise of the option if it is an NSO, and (5) other legal consideration approved by the 2016 Plan administrator.

Tax Limitations on Incentive Stock Options. The aggregate fair market value, determined at the time of grant, of our common stock with respect to ISOs that are exercisable for the first time by the participant during any calendar year under all of our stock plans may not exceed $100,000. Options or portions thereof that exceed such limit will generally be treated as NSOs. No ISO may be granted to any person who, at the time of the grant, owns or is deemed to own stock possessing more than 10% of our total combined voting power or that of any of our affiliates unless (1) the option exercise price is at least 110% of the fair market value of the stock subject to the option on the date of grant, and (2) the term of the ISO does not exceed five years from the date of grant.

Restricted Stock Awards. Restricted stock awards are granted pursuant to restricted stock award agreements adopted by the 2016 Plan administrator. Restricted stock awards may be granted in consideration for (1) cash, check, bank draft or money order, (2) services rendered to us or our affiliates, or (3) any other form of legal consideration. Common stock acquired under a restricted stock award may, but need not, be subject to a share repurchase option in our favor in accordance with a vesting schedule to be determined by the 2016 Plan administrator. A restricted stock award may be transferred only upon such terms and conditions as set by the 2016 Plan administrator. Except as otherwise provided in the applicable award agreement, restricted stock awards that have not vested may be forfeited or repurchased by us upon the participant's cessation of continuous service for any reason.

Restricted Stock Unit Awards. Restricted stock unit awards are granted pursuant to restricted stock unit award agreements adopted by the 2016 Plan administrator. Restricted stock unit awards may be granted in consideration for any form of legal consideration. A restricted stock unit award may be settled by cash, delivery of stock, a combination of cash and stock as deemed appropriate by the 2016 Plan administrator, or in any other form of consideration set forth in the restricted stock unit award agreement. Additionally, dividend equivalents may be credited in respect of shares covered by a restricted stock unit award.

Except as otherwise provided in the applicable award agreement, restricted stock units that have not vested will be forfeited upon the participant's cessation of continuous service for any reason.

Stock Appreciation Rights. Stock appreciation rights are granted pursuant to stock appreciation grant agreements adopted by the 2016 Plan administrator. The 2016 Plan administrator determines the strike price for a stock appreciation right, which generally cannot be less than 100% of the fair market value of our common stock on the date of grant. Upon the exercise of a stock appreciation right, we will pay the participant an amount equal to the product of (1) the excess of the per share fair market value of our common stock on the date of exercise over the strike price, multiplied by (2) the number of shares of common stock with respect to which the stock appreciation right is exercised. A stock appreciation right granted under the 2016 Plan vests at the rate specified in the stock appreciation right agreement as determined by the 2016 Plan administrator.

The 2016 Plan administrator determines the term of stock appreciation rights granted under the 2016 Plan, up to a maximum of ten years. Unless the terms of a participant's stock appreciation right agreement provides

otherwise, if a participant's service relationship with us or any of our affiliates ceases for any reason other than cause, disability or death, the participant may generally exercise any vested stock appreciation right for a period of three months following the cessation of service. The stock appreciation right term may be further extended in the event that exercise of the stock appreciation right following such a termination of service is prohibited by applicable securities laws. If a participant's service relationship with us, or any of our affiliates, ceases due to disability or death, or a participant dies within a certain period following cessation of service, the participant or a beneficiary may generally exercise any vested stock appreciation right for a period of 12 months in the event of disability and 18 months in the event of death. In the event of a termination for cause, stock appreciation rights generally terminate immediately upon the occurrence of the event giving rise to the termination of the individual for cause. In no event may a stock appreciation right be exercised beyond the expiration of its term.

Performance Awards. The 2016 Plan permits the grant of performance-based stock and cash awards that may qualify as performance-based compensation that is not subject to the $1,000,000 limitation on the income tax deductibility of compensation paid to a covered executive officer imposed by Section 162(m) of the Code. To help assure that the compensation attributable to performance-based awards will so qualify, our compensation committee can structure such awards so that stock or cash will be issued or paid pursuant to such award only after the achievement of certain pre-established performance goals during a designated performance period.

The performance goals that may be selected include one or more of the following: ((1) earnings (including earnings per share and net earnings); (2) earnings before interest, taxes and depreciation; (3) earnings before interest, taxes, depreciation and amortization; (4) total stockholder return; (5) return on equity or average stockholder's equity; (6) return on assets, investment, or capital employed; (7) stock price; (8) margin (including gross margin); (9) income (before or after taxes); (10) operating income; (11) operating income after taxes; (12) pre-tax profit; (13) operating cash flow; (14) sales or revenue targets; (15) increases in revenue or product revenue; (16) expenses and cost reduction goals; (17) improvement in or attainment of working capital levels; (18) economic value added (or an equivalent metric); (19) market share; (20) cash flow; (21) cash flow per share; (22) share price performance; (23) debt reduction; (24) customer satisfaction; (25) stockholders' equity; (26) capital expenditures; (27) debt levels; (28) operating profit or net operating profit; (29) workforce diversity; (30) growth of net income or operating income; (31) billings; (32) pre-clinical development related compound goals; (33) financing; (34) regulatory milestones, including approval of a compound; (35) stockholder liquidity; (36) corporate governance and compliance; (37) product commercialization; (38) intellectual property; (39) personnel matters; (40) progress of internal research or clinical programs; (41) progress of partnered programs; (42) partner satisfaction; (43) budget management; (44) clinical achievements; (45) completing phases of a clinical study (including the treatment phase); (46) announcing or presenting preliminary or final data from clinical studies; in each case, whether on particular timelines or generally; (47) timely completion of clinical trials; (48) submission of INDs and NDAs and other regulatory achievements; (49) partner or collaborator achievements; (50) internal controls, including those related to the Sarbanes-Oxley Act of 2002; (51) research progress, including the development of programs; (52) investor relations, analysts and communication; (53) manufacturing achievements (including obtaining particular yields from manufacturing runs and other measurable objectives related to process development activities); (54) strategic partnerships or transactions (including in-licensing and out-licensing of intellectual property; (55) establishing relationships with commercial entities with respect to the marketing, distribution and sale of the Company's products (including with group purchasing organizations, distributors and other vendors); (56) supply chain achievements (including establishing relationships with manufacturers or suppliers of active pharmaceutical ingredients and other component materials and manufacturers of the Company's products); (57) co-development, co-marketing, profit sharing, joint venture or other similar arrangements; and (58) to the extent that an award is not intended to comply with Section 162(m) of the Code, other measures of performance selected by our board of directors.

The performance goals may be based on a company-wide basis, with respect to one or more business units, divisions, affiliates, or business segments, and in either absolute terms or relative to the performance of one or more comparable companies or the performance of one or more relevant indices. Unless specified otherwise (A) in the award agreement at the time the award is granted or (B) in such other document setting forth the

performance goals at the time the goals are established, we will appropriately make adjustments in the method of calculating the attainment of performance goals as follows: (1) to exclude restructuring and/or other nonrecurring charges; (2) to exclude exchange rate effects; (3) to exclude the effects of changes to generally accepted accounting principles; (4) to exclude the effects of any statutory adjustments to corporate tax rates; (5) to exclude the effects of items that are "unusual" in nature or occur "infrequently" as determined under generally accepted accounting principles; (6) to exclude the dilutive effects of acquisitions or joint ventures; (7) to assume that any business divested by the Company achieved performance objectives at targeted levels during the balance of a Performance Period following such divestiture; (8) to exclude the effect of any change in the outstanding shares of common stock of the Company by reason of any stock dividend or split, stock repurchase, reorganization, recapitalization, merger, consolidation, spin-off, combination or exchange of shares or other similar corporate change, or any distributions to common stockholders other than regular cash dividends; (9) to exclude the effects of stock based compensation and the award of bonuses under the Company's bonus plans; (10) to exclude costs incurred in connection with potential acquisitions or divestitures that are required to be expensed under generally accepted accounting principles; and (11) to exclude the goodwill and intangible asset impairment charges that are required to be recorded under generally accepted accounting principles. In addition, we retain the discretion to reduce or eliminate the compensation or economic benefit due upon attainment of the performance goals and to define the manner of calculating the performance criteria we select to use for such performance period. The performance goals may differ from participant to participant and from award to award.

Other Stock Awards. The 2016 Plan administrator may grant other awards based in whole or in part by reference to our common stock. The 2016 Plan administrator will set the number of shares under the stock award and all other terms and conditions of such awards.

Transferability. Unless the 2016 Plan administrator provides otherwise, options generally are not transferable except by will, the laws of descent and distribution, or pursuant to a domestic relations order. A participant may designate a beneficiary, however, who may exercise the option following the participant's death. A participant generally may not transfer other stock awards under our 2016 Plan other than by will, the laws of descent and distribution, or as otherwise provided under our 2016 Plan.

Changes to Capital Structure. In the event that there is a specified type of change in our capital structure, such as a stock split or recapitalization, appropriate adjustments will be made to (1) the class and maximum number of shares reserved for issuance under the 2016 Plan, (2) the class and maximum number of shares by which the share reserve may increase automatically each year, (3) the class and maximum number of shares that may be issued upon the exercise of ISOs, (4) the class and maximum number of shares subject to stock awards that can be granted in a fiscal year (as established under the 2016 Plan pursuant to Section 162(m) of the Code), and (5) the class and number of shares and exercise price, strike price, or purchase price, if applicable, of all outstanding stock awards.

Transactions. The following applies to stock awards under the 2016 Plan in the event of a transaction, unless otherwise provided in a participant's stock award agreement or other written agreement with us or one of our affiliates or in any director compensation policy or unless otherwise expressly provided by the 2016 Plan administrator at the time of grant.

In the event of a transaction (as defined in the 2016 Plan and described below), our board of directors will have the discretion to take one or more of the following actions with respect to outstanding stock awards, contingent upon the closing or completion of such transaction, unless otherwise provided in the stock award agreement or other written agreement with the participant or unless otherwise provided by our board of directors at the time of grant:

- arrange for the surviving or acquiring corporation (or its parent company) to assume or continue the award or to substitute a similar stock award for the award (including an award to acquire the same consideration paid to our stockholders pursuant to the transaction);

- arrange for the assignment of any reacquisition or repurchase rights held by us with respect to the stock award to the surviving or acquiring corporation (or its parent company);
- accelerate the vesting (and, if applicable, the exercisability) in whole or in part of the stock award to a date prior to the effective time of the transaction and provide for its termination at or prior to the effective time of the transaction;
- arrange for the lapse, in whole or in part, of any reacquisition or repurchase rights held by us with respect to the stock award;
- cancel or arrange for the cancellation of the stock award, to the extent not vested or exercised prior to the effective time of the transaction, in exchange for such cash consideration or no consideration, as our board of directors may consider appropriate; and
- make a payment, in such form as may be determined by our board of directors, equal to the excess, if any, of (i) the value of the property the participant would have received upon the exercise of the stock award immediately prior to the effective time of the transaction, over (ii) any exercise price payable in connection with such exercise (for clarity, this payment may be $0 if the value of the property is equal to or less than the exercise price and payments may be delayed to the same extent that payment of consideration to our common stockholders is delayed as a result of escrows, earn outs, holdbacks or any other contingencies).

The board of directors is not obligated to treat all stock awards or portions of stock awards in the same manner. The board of directors may take different actions with respect to the vested and unvested portions of a stock award.

Under the 2016 Plan, a "transaction" means a "corporate transaction" or a "change in control." A corporate transaction is generally the consummation of (1) a sale or other disposition of all or substantially all of our consolidated assets, (2) a sale or other disposition of more than 50% of our outstanding securities, (3) a merger, consolidation or similar transaction following which we are not the surviving corporation, or (4) a merger, consolidation or similar transaction following which we are the surviving corporation but the shares of our common stock outstanding immediately prior to such transaction are converted or exchanged into other property by virtue of the transaction. Under the 2016 Plan, a "change of control" is generally (1) the acquisition by a person or entity of more than 50% of our combined voting power other than by merger, consolidation or similar transaction; (2) a consummated merger, consolidation or similar transaction immediately after which our stockholders cease to own more than 50% of the combined voting power of the surviving entity; or (3) a consummated sale, lease or exclusive license or other disposition of all or substantially all of our consolidated assets.

Change of Control. The 2016 Plan administrator may provide, in an individual award agreement or in any other written agreement between a participant and us that the stock award will be subject to additional acceleration of vesting and exercisability in the event of a change of control. For example, certain of our employees may receive an award agreement that provides for vesting acceleration upon the individual's termination without cause or resignation for good reason (including a material reduction in the individual's base salary, duties, responsibilities or authority, or a material relocation of the individual's principal place of employment with us) in connection with a change of control.

Amendment and Termination. Our board of directors has the authority to amend, suspend, or terminate the 2016 Plan, provided that such action does not materially impair the existing rights of any participant without such participant's written consent. No ISOs may be granted after the tenth anniversary of the date our board of directors adopted the 2016 Plan.

2016 Employee Stock Purchase Plan

Our board of directors adopted our 2016 Employee Stock Purchase Plan (2016 ESPP) in July 2016, and our stockholders approved our 2016 ESPP in July 2016. Our 2016 ESPP will become effective upon the execution and delivery of the underwriting agreement related to this offering. Our 2016 ESPP includes both a component that is intended to qualify as an employee stock purchase plan under Section 423 of the Code and a component that is not intended to so qualify. The purpose of the non-423 component of our 2016 ESPP is to authorize the grant of purchase rights that do not meet the requirements of an employee stock purchase plan to achieve tax, regulatory or other objectives.

The first offering period under our 2016 ESPP will begin and end upon a date to be approved by our board of directors or the compensation committee.

Authorized Shares. The maximum aggregate number of shares of our common stock that may be issued under our 2016 ESPP is 150,000 shares. Additionally, the number of shares of our common stock reserved for issuance under our 2016 ESPP will automatically increase on the first day of each fiscal year for ten years, beginning on the fiscal year following the fiscal year in which the 2016 Plan becomes effective, in an amount equal to the lesser of (1) 1% of the total number of shares of our capital stock outstanding on the last day of the preceding fiscal year; (2) 300,000 shares of common stock; or (3) such lesser number as determined by our board of directors. The stock purchasable under the 2016 ESPP will be shares of authorized but unissued or reacquired common stock, including shares repurchased by us in the open market. Shares subject to purchase rights granted under our 2016 ESPP that terminate without having been exercised in full will be available for grant under our 2016 ESPP.

Plan Administration. Our board of directors will administer our 2016 ESPP. Our board of directors may delegate authority to administer our 2016 ESPP to our compensation committee.

Subject to the terms of the 2016 ESPP, our board of directors or the authorized committee, referred to here as the 2016 ESPP administrator, may approve offerings with a duration of not more than 27 months, and may specify one or more shorter purchase periods within each offering. Each offering will have one or more purchase dates on which shares of our common stock will be purchased for the employees who are participating in the offering. The administrator, in its discretion, will determine the terms of offerings under our 2016 ESPP including determining which of our designated affiliates will be eligible to participate in the 423 component of our 2016 ESPP and which of our designated affiliates will be eligible to participate in the non-423 component of our 2016 ESPP.

Eligibility. Our employees, including executive officers, may have to satisfy one or more of the following service requirements before participating in our 2016 ESPP, as determined by the administrator: (1) customary employment for more than 20 hours per week and more than five months per calendar year, or (2) continuous employment for a minimum period of time, not to exceed two years. An employee may not be granted rights to purchase stock under our 2016 ESPP if such employee (a) immediately after the grant would own stock possessing 5% or more of the total combined voting power or value of our common stock or (b) holds rights to purchase stock under our 2016 ESPP that would accrue at a rate that exceeds $25,000 worth of our stock for each calendar year that the rights remain outstanding.

Purchase Rights and Purchase Price. Our 2016 ESPP permits participants to purchase shares of our common stock through payroll deductions or other methods with up to 15% of their earnings. The purchase price of the shares will be not less than 85% of the lower of the fair market value of our common stock on the first day of an offering or on the date of purchase.

Purchase of Stock. In connection with offerings made under the 2016 ESPP, the Board may specify a maximum number of shares of common stock an employee may be granted the right to purchase and the maximum aggregate number of shares of common stock that may be purchased pursuant to such offering by all

participants. If the aggregate number of shares to be purchased upon exercise of all outstanding purchase rights would exceed the number of shares of common stock remaining available under the 2016 ESPP, or the maximum number of shares that may be purchased on a single purchase date across all offerings, the Board would make a pro rata allocation (based on each participant's accumulated payroll deductions) of available shares. Unless the employee's participation is discontinued, the employee's right to purchase shares is exercised automatically at the end of the purchase period at the applicable price.

Withdrawal. While each participant in the 2016 ESPP is required to sign an agreement authorizing payroll deductions, the participant may withdraw from a given offering by terminating the employee's payroll deductions and by delivering to us a notice of withdrawal from the 2016 ESPP. Such withdrawal may be elected at any time prior to the end of the applicable offering, except as otherwise provided in the offering.

Upon any withdrawal from an offering by the employee, we will distribute to the employee the employee's accumulated payroll deductions without interest, less any accumulated deductions previously applied to the purchase of shares of common stock on the employee's behalf during such offering, and such employee's rights in the offering will be automatically terminated. The employee is not entitled to again participate in that offering. However, an employee's withdrawal from an offering will not prevent such employee from participating in subsequent offerings under the 2016 ESPP.

Reset Feature. Our board of directors has the authority to provide that if the fair market value of a share of our common stock on the first day of any purchase period within a particular offering period is less than or equal to the fair market value on the start date of that offering period, then the participants in that offering period will automatically be transferred and enrolled in a new offering period which will begin on the first day of that purchase period and the participants' purchase rights in the original offering period will terminate.

Termination of Employment. Unless otherwise specified by our board of directors, a participant's rights under any offering under the 2016 ESPP terminate immediately upon cessation of an employee's employment for any reason (subject to any post-employment participation period required by law), and we will distribute to such employee all of the employee's accumulated payroll deductions, without interest.

Transferability. A participant may not transfer purchase rights under our 2016 ESPP other than by will, the laws of descent and distribution, or as otherwise provided under our 2016 ESPP.

Changes to Capital Structure. In the event that there is a specified type of change in our capital structure, such as a stock split or recapitalization, (i) the class and maximum number of securities subject to the 2016 ESPP, (ii) the class and maximum number of securities by which the share reserve is to increase automatically each year, (iii) the class and number of securities subject to, and the purchase price applicable to outstanding offerings and purchase rights, and (iv) the class and number of securities that are the subject of the purchase limits under each ongoing offering.

Corporate Transactions. In the event of a specified corporate transaction, such as a merger or change in control, a successor corporation may assume, continue or substitute each outstanding purchase right. If the successor corporation does not assume, continue or substitute for the outstanding purchase rights, the offering in progress may be shortened and a new exercise date will be set, so that the participants' purchase rights can be exercised and terminate immediately thereafter.

Plan Amendment or Termination. Our board of directors has the authority to amend, suspend or terminate our 2016 ESPP, at any time and for any reason. Any benefits, privileges, entitlements and obligations under any outstanding purchase rights granted before an amendment, suspension or termination of the 2016 ESPP will not be materially impaired except (1) with the participant's consent; (2) to comply with any laws, listing requirements, or regulations; or (3) to obtain or maintain favorable tax, listing or regulatory treatment.

Perquisites, Health, Welfare and Retirement Benefits

Our named executive officers are eligible to participate in our employee benefit plans, including our medical, dental, vision, group life, disability and accidental death and dismemberment insurance plans, in each case on the same basis as all of our other employees. In addition, we provide a medical cash subsidy to any employee, including a named executive officer, who chooses not to participate in our benefit plans described above. We provide a 401(k) plan to our employees, including our named executive officers, as discussed in the section below entitled "—401(k) Plan."

We generally do not provide perquisites or personal benefits to our named executive officers, except in limited circumstances. We do, however, pay the premiums for term life insurance and disability insurance for all of our employees, including our current named executive officers.

401(k) Plan

We maintain a defined contribution employee retirement plan that provides eligible U.S. employees with an opportunity to save for retirement on a tax advantaged basis under Section 401(k) of the Code. Eligible employees may defer eligible compensation subject to applicable annual Code limits. The 401(k) plan permits participants to make both pre-tax and certain after-tax deferral contributions. These contributions are allocated to each participant's individual account and are then invested in selected investment alternatives according to the participant's directions. Earnings on those contributions are not taxable to the employees until distributed from the 401(k) plan. Employees are immediately and fully vested in their contributions. Currently, we do not make matching contributions or discretionary contributions to the 401(k) plan.

Nonqualified Deferred Compensation

We do not maintain any nonqualified deferred compensation plans. Our board of directors may elect to provide our officers and other employees with nonqualified deferred compensation benefits in the future if it determines that doing so is in our best interests.

Limitations of Liability and Indemnification Matters

Our amended and restated certificate of incorporation and our amended and restated bylaws provide that we will indemnify our directors and officers to the fullest extent permitted by the Delaware General Corporation Law, which prohibits our amended and restated certificate of incorporation from limiting the liability of our directors for the following:

- any breach of the director's duty of loyalty to us or our stockholders;
- acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law;
- unlawful payment of dividends or unlawful stock repurchases or redemptions; or
- any transaction from which the director derived an improper personal benefit.

Our amended and restated certificate of incorporation and our amended and restated bylaws also provide that if Delaware law is amended to authorize corporate action further eliminating or limiting the personal liability of a director, then the liability of our directors will be eliminated or limited to the fullest extent permitted by Delaware law, as so amended. This limitation of liability does not apply to liabilities arising under the federal securities laws and does not affect the availability of equitable remedies such as injunctive relief or rescission.

Our amended and restated certificate of incorporation and our amended and restated bylaws also provide that we shall have the power to indemnify our employees and agents to the fullest extent permitted by law. Our amended and restated bylaws also permit us to secure insurance on behalf of any officer, director, employee or

other agent for any liability arising out of his or her actions in this capacity, regardless of whether our amended and restated bylaws would permit indemnification. We have obtained directors' and officers' liability insurance.

We have entered into separate indemnification agreements with our directors and executive officers, in addition to indemnification provided for in our amended and restated certificate of incorporation and amended and restated bylaws. These agreements, among other things, provide for indemnification of our directors and executive officers for expenses, judgments, fines and settlement amounts incurred by this person in any action or proceeding arising out of this person's services as a director or executive officer or at our request. We believe that these provisions in our amended and restated certificate of incorporation and amended and restated bylaws and indemnification agreements are necessary to attract and retain qualified persons as directors and executive officers.

The above description of the indemnification provisions of our amended and restated certificate of incorporation, our amended and restated bylaws and our indemnification agreements is not complete and is qualified in its entirety by reference to these documents, each of which is filed as an exhibit to the registration statement of which this prospectus is a part.

The limitation of liability and indemnification provisions in our amended and restated certificate of incorporation and amended and restated bylaws may discourage stockholders from bringing a lawsuit against directors for breach of their fiduciary duties. They may also reduce the likelihood of derivative litigation against directors and officers, even though an action, if successful, might benefit us and our stockholders. A stockholder's investment may be harmed to the extent we pay the costs of settlement and damage awards against directors and officers pursuant to these indemnification provisions. Insofar as indemnification for liabilities under the Securities Act may be permitted to directors, officers or persons controlling us pursuant to the foregoing provisions, we have been informed that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable. There is no pending litigation or proceeding naming any of our directors or officers as to which indemnification is being sought, nor are we aware of any pending or threatened litigation that may result in claims for indemnification by any director or officer.

CERTAIN RELATIONSHIPS AND RELATED PERSON TRANSACTIONS

The following includes a summary of transactions since January 1, 2013 to which we have been a party in which the amount involved exceeded or will exceed $120,000, and in which any of our directors, executive officers or, to our knowledge, beneficial owners of more than 5% of our capital stock or any member of the immediate family of any of the foregoing persons had or will have a direct or indirect material interest, other than equity and other compensation, termination, change in control and other arrangements, which are described under "Executive Compensation." We also describe below certain other transactions with our directors, executive officers and stockholders. We believe the terms obtained or consideration that we paid or received, as applicable, in connection with the transactions described below were comparable to terms available or the amounts that would be paid or received, as applicable, in arm's-length transactions with unrelated third parties.

Preferred Stock Financings

Series B Preferred Stock Financing

In May 2013 and August 2014, we issued and sold an aggregate of 36,000,000 shares of our Series B preferred stock (Series B Stock), at a purchase price of $0.50 per share, for aggregate consideration of approximately $18.0 million. In connection with this preferred stock financing, we also issued warrants to purchase an aggregate of 4,000,000 shares of our Series B Stock at an exercise price of $0.01 per share (Series B Warrants). In April 2016, Series B Warrants were exercised for 1,999,998 shares of Series B Stock. The outstanding Series B Warrants expire in May 2016.

The participants in this preferred stock financing included the following holders of more than 5% of our capital stock or entities affiliated with them. The following table sets forth the aggregate number of shares of Series B Stock issued to these related parties in this preferred stock financing:

Participants	Shares of Series B Stock	Warrants to Purchase Shares of Series B Stock	Aggregate Purchase Price
Johnson & Johnson Development Corporation	14,000,000	—	$ 7,000,000
Lilly Ventures Fund I, LLC(1).	8,000,000	2,285,714	4,000,000
Pharmstandard International S.A.	8,000,000	—	4,000,000
Entities affiliated with Starfish Technology Fund(2)	6,000,000	1,714,286	3,000,000
Total	36,000,000	4,000,000	$18,000,000

(1) Armen B Shanafelt, Ph.D. is a member of our board of directors who was designated by Lilly Ventures Fund I, LLC.

(2) Consists of (a) 4,975,308 shares and warrants to purchase 1,421,517 shares purchased by Starfish Technology Fund 1 LP and (b) 1,024,692 shares and warrants to purchase 292,769 shares purchased by Starfish Pre-Seed Fund.

Series C Preferred Stock Financing

From July 2015 through March 2016, we issued and sold an aggregate of 80,337,411 shares of our Series C preferred stock (Series C Stock), at a purchase price of $0.4979 per share, for aggregate consideration of approximately $40.0 million.

The participants in this preferred stock financing included the following holders of more than 5% of our capital stock or entities affiliated with them. The following table sets forth the aggregate number of shares of Series C Stock issued to these related parties in this preferred stock financing:

Participants	Shares of Series C Stock	Aggregate Purchase Price
Canaan X L.P[1].	27,113,877	$13,500,000
Johnson & Johnson Development Corporation	13,054,830	6,500,000
Adage Capital Partners, LP	12,050,612	6,000,000
Entities affiliated with RA Capital Healthcare Fund, L.P.[2]	10,042,176	4,999,999
Lilly Ventures Fund I, LLC[3]	9,841,333	4,900,000
Pharmstandard International, S.A.	3,012,652	1,500,000
Starfish Technology Fund 1, LP	200,843	100,000
Total	75,316,323	$37,499,999

(1) Consists of 27,113,877 shares of Series C preferred stock purchased by Canaan X L.P. Julie Papanek, a member of our board of directors, is a non-managing member of Canaan Partners X LLC, the general partner of Canaan X L.P. Ms. Papanek does not have voting or investment power over any of the shares directly held by Canaan X L.P.

(2) Consists of (a) 8,264,711 shares purchased by RA Capital Healthcare Fund, L.P. and (b) 1,777,465 shares purchased by Blackwell Partners LLC – Series A.

(3) Armen B Shanafelt, Ph.D. is a member of our board of directors who was designated by Lilly Ventures Fund I, LLC.

Letter Agreement with Johnson & Johnson Development Corporation

In May 2013, in connection with our sale of Series B Stock, we entered into a letter agreement with Johnson & Johnson Development Corporation (JJDC), as amended on April 19, 2016, pursuant to which we granted JJDC a right of first negotiation with respect to the consummation of any proposed sale, transfer, license, commercialization or distribution arrangement (each, a Transaction) of our inventions, developments, patents, patent applications, know-how or other proprietary rights or products controlled by the Company which are necessary for the research, development or commercialization of the PTG-100, PTG-200 and IL-13 programs (each, a Program) other than an acquisition, merger, consolidation, or sale of substantially all of our assets. The letter agreement does not apply with respect to the PTG-300 program. The term of JJDC's right of first negotiation commenced in May 2014 and terminates, with respect to any Program, 60 days after our filing of an IND (or the foreign equivalent), with respect to each Program (the ROFN Period). On November 1, 2015, JJDC waived their right of first negotiation with respect to PTG-100. Neither we, nor JJDC, have an obligation to enter into a Transaction during the Right of First Negotiation Period. Neither we, nor JJDC, have an obligation to enter into a Transaction during the ROFN Period. The Company is not currently pursuing an IL-13 Program.

In the event that we receive a bona fide term sheet for a Program, we are obligated to notify JJDC of such offer (but not the terms thereof) and JJDC has a period of 30 days to notify us of exercise of its right to negotiate for a Transaction with JJDC. Following expiration of the ROFN Period with respect to any remaining Program, we are required to deliver to JJDC certain information relating to such Program, including pre-clinical results, manufacturing protocols and other information relevant to the evaluation of such Program, as determined by us. For a period of 60 days following delivery of such information (the Exclusive Negotiation Period), we are required to negotiate in good faith and exclusively with JJDC to enter into a Transaction with JJDC with respect to such Program and we are not permitted to enter into negotiations with any third party with respect to a Transaction involving such Program that would impair the ability of JJDC to exercise its rights under the letter agreement.

Finally, for a period of 180 days following expiration of an Exclusive Negotiation Period for a Program (the Tail Period), we are not permitted to enter into any a Transaction with respect to such Program with a third party on terms that contain upfront payments and pre-launch milestones (valued on a risk-adjusted basis) that are inferior in total economic value to those that JJDC and its affiliates last offered to us, to the extent any such offer was previously made by JJDC or its affiliates to us.

JJDC's right of first negotiation with respect to any Program that has not earlier expired or been waived by JJDC will terminate upon the sale, transfer or other disposition by us of all or substantially all of our assets, our consummation of a merger or consolidation with or into another entity, or the transfer (whether by merger, consolidation, equity financing, or otherwise), in one transaction or a series of related transactions, to a person or group of affiliated persons a majority or more of our outstanding voting stock (or the surviving or acquiring entity).

Amended and Restated Voting Agreement

We have entered into an amended and restated Voting Agreement, as amended, with certain holders of our common stock and preferred stock, including certain of our named executive officers and directors and entities with which certain of our directors are affiliated, with respect to the election of our directors and certain other matters. All of our current directors were elected pursuant to the terms of this agreement. The amended and restated voting agreement will terminate upon the closing of this offering. For more information, see "Management—Board Composition."

Amended and Restated Right of First Refusal and Co-Sale Agreement

We have entered into an amended and rested right of first refusal and co-sale agreement with certain holders of our common stock and preferred stock, including certain of our named executive officers and directors and entities with which certain of our directors are affiliated. This agreement provides the holders of preferred stock a right of purchase and a right of co-sale in respect of sales of securities by certain holders of our common stock and preferred stock. These rights of purchase and co-sale will terminate upon the closing of this offering.

Amended and Restated Investors' Rights Agreement

We have entered into an amended and restated investors' rights agreement with certain holders of our preferred stock, including certain of our directors and entities with which certain of our directors are affiliated. This agreement provides that the holders of common stock issuable upon conversion of our preferred stock have the right to demand that we file a registration statement or request that their shares of common stock be covered by a registration statement that we are otherwise filing. With respect to this offering, the registration rights have been validly waived. In addition to the registration rights, the amended and restated investors' rights agreement provides for certain information rights and a right of first offer. The provisions of the amended and restated investors' rights agreement, other than those relating to registration rights, will terminate upon the closing of this offering. For more information regarding this agreement, see "Description of Capital Stock—Registration Rights."

Certain of our existing stockholders and their affiliated entities, including investors affiliated with certain of our directors, have indicated an interest in purchasing an aggregate of up to approximately $40.0 million in shares of our common stock in this offering at the initial public offering price and on the same terms as the other purchasers in this offering. However, because indications of interest are not binding agreements or commitments to purchase, these investors may determine to purchase fewer shares than they indicate an interest in purchasing or not to purchase any shares in this offering. It is also possible that these investors could indicate an interest in purchasing more shares of our common stock. In addition, the underwriters could determine to sell fewer shares to any of these investors than the investors indicate an interest in purchasing or not to sell any shares to these investors.

Indemnification Agreements

We have entered into indemnification agreements with each of our directors and executive officers prior to the completion of this offering. These agreements, among other things, require us or will require us to indemnify each director (and in certain cases their related venture capital funds) and executive officer to the fullest extent permitted by Delaware law, including indemnification of expenses such as attorneys' fees, judgments, fines and settlement amounts incurred by the director or executive officer in any action or proceeding, including any action or proceeding by or in right of us, arising out of the person's services as a director or executive officer.

Our amended and restated certificate of incorporation and our amended and restated bylaws provide that we will indemnify each of our directors and officers to the fullest extent permitted by the Delaware General Corporation Law. Further, we have entered into indemnification agreements with each of our directors and officers, and we have purchased a policy of directors' and officers' liability insurance that insures our directors and officers against the cost of defense, settlement or payment of a judgment under certain circumstances. For further information, see "Executive Compensation—Limitations of Liability and Indemnification Matters."

Policies and Procedures for Related Person Transactions

Our board of directors will adopt a written related person transaction policy, to be effective upon the completion of this offering, setting forth the policies and procedures for the review and approval or ratification of related-person transactions. This policy will cover, with certain exceptions set forth in Item 404 of Regulation S-K under the Securities Act, any transaction, arrangement or relationship, or any series of similar transactions, arrangements or relationships in which we were or are to be a participant, where the amount involved exceeds $120,000 and a related person had or will have a direct or indirect material interest, including, without limitation, purchases of goods or services by or from the related person or entities in which the related person has a material interest, indebtedness, guarantees of indebtedness and employment by us of a related person. In reviewing and approving any such transactions, our audit committee is tasked to consider all relevant facts and circumstances, including, but not limited to, whether the transaction is on terms comparable to those that could be obtained in an arm's length transaction and the extent of the related person's interest in the transaction. All of the transactions described in this section occurred prior to the adoption of this policy.

PRINCIPAL STOCKHOLDERS

The following table sets forth information with respect to the beneficial ownership of our common stock as of June 30, 2016, and as adjusted to reflect the sale of shares of common stock in this offering, by:

- each of our named executive officers;
- each of our directors;
- all of our executive officers and directors as a group; and
- each person or group of affiliated persons known by us to beneficially own more than 5% of our common stock.

The number of shares beneficially owned by each stockholder is determined under rules issued by the SEC. Under these rules, beneficial ownership includes any shares as to which a person has sole or shared voting power or investment power.

The percentage ownership information under the column titled "Before Offering" is based on 8,961,481 shares of common stock outstanding as of June 30, 2016, assuming conversion of all outstanding shares of our preferred stock into 8,577,571 shares of common stock upon the closing of this offering. The percentage ownership information under the column titled "After Offering" is based on the sale of 14,796,481 shares of common stock outstanding immediately after the closing in this offering (assuming an initial public offering price of $12.00 per share, the midpoint of the price range set forth on the cover page of this prospectus). The percentage ownership information assumes no exercise of the underwriters' option to purchase additional shares.

Information with respect to beneficial ownership has been furnished by each director, officer or beneficial owner of more than 5% of our common stock. We have determined beneficial ownership in accordance with the rules of the SEC. These rules generally attribute beneficial ownership of securities to persons who possess sole or shared voting power or investment power with respect to those securities. In addition, the rules include shares of our common stock issuable pursuant to the exercise of stock options or warrants that are either immediately exercisable or exercisable within 60 days of June 30, 2016. Unless otherwise indicated, we believe, based on the information furnished to us, that the persons or entities identified in this table have sole voting and investment power with respect to all shares shown as beneficially owned by them, subject to applicable community property laws. This information does not necessarily indicate beneficial ownership for any other purpose, including for purposes of Sections 13(d) and 13(g) of the Securities Act.

Certain of our existing stockholders and their affiliated entities, including investors affiliated with certain of our directors, have indicated an interest in purchasing an aggregate of up to approximately $40.0 million in shares of our common stock in this offering at the initial public offering price and on the same terms as the other purchasers in this offering. However, because indications of interest are not binding agreements or commitments to purchase, any of these stockholders may determine to purchase more, less or no shares in this offering, or the underwriters may determine to sell more, less or no shares in this offering to any of these stockholders. The following table does not reflect any potential purchases by these stockholders, which purchases, if any, will increase the percentage of shares owned after the offering of such stockholder from that set forth in the table below.

Unless otherwise indicated, the address of each beneficial owner listed below is c/o Protagonist Therapeutics, Inc., 521 Cottonwood Drive, Suite 100, Milpitas, California 95035.

Name of Beneficial Owner	Number of Shares Beneficially Owned		Percentage of Shares Beneficially Owned	
	Before Offering	After Offering	Before Offering	After Offering
5% Stockholders				
Canaan X L.P.[1]	1,869,922	1,869,922	20.9%	12.6%
Johnson & Johnson Development Corporation[2]	1,865,850	1,865,850	20.8%	12.6%
Lilly Ventures Fund I, LLC[3]	1,516,149	1,516,149	16.9%	10.2%
Adage Capital Partners, LP[4]	831,076	831,076	9.3%	5.6%
Pharmstandard International, S.A.[5]	759,493	759,493	8.5%	5.1%
Entities affiliated with Starfish Technology Fund[6]	696,237	696,237	7.8%	4.7%
RA Capital Healthcare Fund, L.P.[7]	692,563	692,563	7.7%	4.7%
Executive Officers and Directors				
Dinesh V. Patel, Ph.D.[8]	177,354	177,354	2.0%	1.2%
David Y. Liu, Ph.D.[9]	41,652	41,652	*	*
William Hodder[10]	14,423	14,423	*	*
Harold E. Selick, Ph.D.[11]	16,596	16,596	*	*
Chaitan Khosla, Ph.D.[12]	8,390	8,390	*	*
Julie Papanek[13]	—	—	—	—
Armen B. Shanafelt, Ph.D.[3]	1,516,149	1,516,540	16.9%	10.2%
William D. Waddill	540	540	*	*
All executive officers and directors as a group (10 persons)[14]	1,775,104	1,775,104	19.05%	11.9%

* Represents beneficial ownership of less than one percent.

(1) Consists of 1,869,922 shares of common stock issuable upon conversion of Series C redeemable convertible preferred stock held by Canaan X L.P. Canaan Partners X LLC is the general partner of Canaan X L.P. and may be deemed to have sole investment and voting power over the shares held by Canaan X L.P. Brenton K. Ahrens, Stephen M. Bloch, Daniel T. Ciporin, Wende S. Hutton, Maha S. Ibrahim, Deepak Kamra, Nina Kjellson, Guy M. Russo, Tim Shannon and Hrach Simonian are the managing members of Canaan Partners X LLC. Investment, voting and dispositive decisions with respect to the shares held by Canaan X L.P. are made by the managers of Canaan Partners X LLC, collectively. Julie Papanek is a non-managing member of Canaan Partners X LLC, the general partner of Canaan X L.P., and a member of our board of directors. Neither any manager of Canaan Partners X LLC nor Ms. Papanek has beneficial ownership (within the meaning of Rule 13d-3 promulgated under the Exchange Act) of any shares held by Canaan X L.P. The address for Canaan X L.P. is 285 Riverside Avenue, Suite 250, Westport, CT 06880.

(2) The board of directors of JJDC, which consists of Paulus Stoffels and Steven Rosenberg, has shared investment and voting control with respect to the shares held by JJDC and has delegated responsibility therefor to the management of JJDC to take such actions on behalf of JJDC. As such, no individual member of the JJDC board of directors is deemed to hold any beneficial ownership or reportable pecuniary interest in the shares held by JJDC. No individual representative of JJDC shall be deemed (i) a beneficial owner of, or (ii) to have a reportable pecuniary interest in, the shares held by JJDC. The address of JJDC is 410 George Street, New Brunswick, NJ 08901

(3) As such, LVMG may be deemed to indirectly beneficially own the shares held by LVFI. LVMG's voting and dispositive decisions with respect to the shares held by LVFI are made by LVMG's management committee, which consists of Ed Torres, Steve Hall and Armen Shanafelt (collectively, the Management Committee Members). The members of LVFI consist of the Management Committee Members and Eli Lilly and Company. However, Eli Lilly and Company has no voting or dispositive power with respect to the shares held by LVFI. The mailing addresses of the beneficial owners is 115 West Washington Street, Suite 1680-South, Indianapolis, IN 46204.

(4) Adage Capital Partners, GP, LLC (ACPGP) serves as the general partner of Adage Capital Partners, LP (ACPLP) and as such has discretion over the portfolio of securities beneficially owned by ACPLP. Adage Capital Advisors, LLC (ACA)

is the managing member of ACPGP and directs ACPGP's operations. Robert Atchinson and Phillip Gross are the managing members of ACA. Mr. Atchinson and Mr. Gross disclaim beneficial ownership of the reported securities except to the extent of their pecuniary interest therein. The address of Adage Capital Partners, L.P. is 200 Clarendon Street, 52nd Floor, Boston, Massachusetts 02110.

(5) Pharmstandard International S.A (Pharmstandard) is a wholly owned subsidiary of Public Joint Stock Company "Pharmstandard." As the parent entity, Public Joint Stock Company "Pharmstandard" has voting and investment control over the shares of the Company held by Pharmstandard. The address of Pharmstandard is 65, Boulevard Grande Duchesse Charlotte, L-1331 Luxembourg, Grand Duchy of Luxembourg.

(6) Consists of (a) 579,699 shares held by Starfish Technology Fund I LP and (b) 116,538 shares held Starfish Ventures Pty Ltd, as the responsible entity of the Starfish Pre-Seed Fund. The general partner of the Starfish Technology Fund I LP is Starfish Management Company I Pty Ltd, which is wholly-owned by Starfish Ventures Pty Ltd. Starfish Management Company I Pty Ltd has appointed Starfish Ventures Pty Ltd as manager of the Starfish Technology Fund I LP and Starfish Ventures Pty Ltd has the power to bind Starfish Technology Fund I LP and Starfish Pre-Seed Fund. Michael Panaccio and John Dyson are the only directors of the Starfish Ventures Pty Ltd. The registered address of Starfish Ventures Pty Ltd is c/o Chambers & Partners Lv 4, 437 St Kilda Road, Melbourne, Australia, 3004.

(7) Consists of 569,980 shares held by RA Capital Healthcare Fund, L.P. and 122,583 shares held by Blackwell Partners LLC – Series A. The investment adviser and sole general partner of RA Capital Healthcare Fund, LP and Blackwell Partners LLC – Series A is RA Capital Management, LLC. Peter Kolchinsky is the sole managing member of RA Capital Management, LLC and has the power to vote or dispose of the shares held by RA Capital Healthcare Fund, LP. The address for Dr. Kolchinsky, RA Capital Healthcare Fund, LP and Blackwell Partners LLC – Series A is 20 Park Plaza, Suite 1200, Boston, MA 02116.

(8) Includes 45,378 shares issuable pursuant to stock options exercisable within 60 days of June 30, 2016.

(9) Consists of 41,652 shares issuable pursuant to stock options exercisable within 60 days of June 30, 2016.

(10) Includes 6,480 shares issuable pursuant to stock options exercisable within 60 days of June 30, 2016.

(11) Consists of 16,596 shares issuable pursuant to stock options exercisable within 60 days of June 30, 2016.

(12) Consists of 8,390 shares issuable pursuant to stock options exercisable within 60 days of June 30, 2016.

(13) Julie Papanek is a non-managing member of Canaan Partners X LLC, the general partner of Canaan X L.P. Ms. Papanek does not have voting or investment power over any of the shares directly held by Canaan X L.P. referenced in footnote (1) above. Ms. Papanek's business address is 285 Riverside Avenue, Suite 250, Westport, Connecticut 06880.

(14) Includes 119,036 shares issuable pursuant to stock options exercisable within 60 days of June 30, 2016.

DESCRIPTION OF CAPITAL STOCK

General

Following the completion of this offering, our authorized capital stock will consist of 90,000,000 shares of common stock, $0.00001 par value per share, and 10,000,000 shares of preferred stock, $0.00001 par value per share.

The following is a summary of the rights of our common and preferred stock and some of the provisions of our amended and restated certificate of incorporation and amended and restated bylaws, which will each become effective upon the closing of this offering, the investors' rights agreement and relevant provisions of Delaware General Corporation Law. Because it is only a summary, it does not contain all the information that may be important to you. For a complete description you should refer to our amended and restated certificate of incorporation, amended and restated bylaws and investors' rights agreement, copies of which have been filed as exhibits to the registration statement of which this prospectus is a part, as well as the relevant provisions of Delaware General Corporation Law.

Common Stock

As of March 31, 2016, there were 8,823,551 shares of our common stock outstanding and held of record by 26 stockholders, assuming the conversion of all outstanding shares of our convertible preferred stock into shares of common stock upon completion of this offering.

Voting Rights

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

Dividend Rights

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

Liquidation

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

Rights and Preferences

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

Fully Paid and Nonassessable

All outstanding shares of common stock are, and the common stock to be outstanding upon the completion of this offering will be, duly authorized, validly issued, fully paid and nonassessable.

Preferred Stock

As of March 31, 2016, there were 122,374,911 shares of our preferred stock outstanding, which will convert into 8,439,641 shares of our common stock upon the closing of this offering.

Upon completion of this offering, all of our previously outstanding shares of redeemable convertible preferred stock will have been converted into common stock, there will be no authorized shares of our previously redeemable convertible preferred stock and we will have no shares of preferred stock outstanding. Under the terms of our amended and restated certificate of incorporation, which will become effective immediately prior to the completion of this offering, our board of directors has the authority, without further action by our stockholders, to issue up to 10,000,000 shares of preferred stock in one or more series, to establish from time to time the number of shares to be included in each such series, to fix the dividend, voting and other rights, preferences and privileges of the shares of each wholly unissued series and any qualifications, limitations or restrictions thereon, and to increase or decrease the number of shares of any such series, but not below the number of shares of such series then outstanding.

Our board of directors may authorize the issuance of preferred stock with voting or conversion rights that could adversely affect the voting power or other rights of the holders of the common stock. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions and other corporate purposes, could, among other things, have the effect of delaying, deferring or preventing a change in our control and may adversely affect the market price of the common stock and the voting and other rights of the holders of common stock. We have no current plans to issue any shares of preferred stock.

Options

As of March 31, 2016, options to purchase 783,341 shares of our common stock were outstanding under our 2007 Stock Option Plan, of which 172,236 were vested and exercisable as of that date.

Warrants

As of March 31, 2016, warrants to purchase 4,000,000 shares of our Series B Stock were outstanding with a weighted average exercise price of $0.01 per share. In April 2016, Series B Warrants were exercised for 1,999,998 shares of Series B Stock. The remaining outstanding warrants expired in May 2016.

Registration Rights

We are party to an amended and restated investors' rights agreement that provides that holders of our preferred stock, including certain holders of 5% of our capital stock and entities affiliated with certain of our directors, have certain registration rights, as set forth below. The registration of shares of our common stock pursuant to the exercise of registration rights described below would enable the holders to sell these shares without restriction under the Securities Act when the applicable registration statement is declared effective. We will pay the registration expenses, other than the underwriting discounts and commissions, of the shares registered pursuant to the demand, piggyback and Form S-3 registrations described below.

Generally, in an underwritten offering, the managing underwriter, if any, has the right, subject to specified conditions, to limit the number of shares such holders may include. The demand, piggyback and Form S-3 registration rights described below will expire upon the earlier of three years following the completion of this offering, or when all investors, considered with their affiliates, can sell all of their shares in a 90-day period under Rule 144.

Demand Registration Rights—The holders of an aggregate of approximately 8.7 million shares of common stock outstanding as of March 31, 2016, issuable upon conversion of outstanding preferred stock and shares of convertible preferred stock issuable upon exercise of outstanding warrants, giving effect to the

company conversion and exercise of such warrants as if it occurred on such date, will be entitled to certain demand registration rights. At any time beginning six months following the date of this prospectus, the holders of a majority of these shares may, on not more than two occasions, request that we register all or a portion of their shares, subject to certain specified exceptions.

Piggyback Registration Rights—In connection with this offering, the holders of an aggregate of approximately 8.7 million shares of common stock outstanding as of March 31, 2016, issuable upon conversion of outstanding preferred stock and shares of convertible preferred stock issuable upon exercise of outstanding warrants, giving effect to the company conversion and exercise of such warrants as if it occurred on such date, were entitled to, and the necessary percentage of holders waived, their rights to notice of this offering and to include their shares of registrable securities in this offering. In the event that we propose to register any of our securities under the Securities Act in another offering, either for our own account or for the account of other security holders, the holders of these shares will be entitled to certain "piggyback" registration rights allowing them to include their shares in such registration, subject to certain marketing and other limitations. As a result, whenever we propose to file a registration statement under the Securities Act, including a registration statement on Form S-3 as discussed below, other than with respect to a demand registration or a registration statement on Forms S-4 or S-8 or related to stock issued upon conversion of debt securities, the holders of these shares are entitled to notice of the registration and have the right, subject to limitations that the underwriters may impose on the number of shares included in the registration, to include their shares in the registration. However, in no event shall the aggregate value of securities of the selling stockholders included in the offering be reduced below twenty-five percent of the total value of all of securities included in such offering.

Form S-3 Registration Rights—The holders of an aggregate of approximately 8.7 million shares of our common stock outstanding as of March 31, 2016, issuable upon conversion of outstanding preferred stock and shares of convertible preferred stock issuable upon exercise of outstanding warrants, giving effect to the company conversion and exercise of such warrants as if it occurred on such date, will be entitled to certain Form S-3 registration rights, provided that we have not already effected two such registrations within the twelve-month period preceding the date of such request. Such holders may make a request that we register their shares on Form S-3 if we are qualified to file a registration statement on Form S-3. Such request for registration on Form S-3 must cover securities the aggregate offering price of which, before payment of underwriting discounts and commissions, is at least $2.5 million.

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

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

These provisions, summarized below, are intended to discourage coercive takeover practices and inadequate takeover bids. These provisions are also designed to encourage persons seeking to acquire control of us to first negotiate with our board of directors. We believe that the benefits of the increased protection of our potential ability to negotiate with the proponent of an unfriendly or unsolicited proposal to acquire or restructure us outweigh the disadvantages of discouraging these proposals because negotiation of these proposals could result in an improvement of their terms.

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

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

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

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

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

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

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

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

Choice of Forum—Our restated certificate of incorporation provides that, unless we consent in writing to the selection of an alternative form, the Court of Chancery of the State of Delaware will be the sole and exclusive forum for: (1) any derivative action or proceeding brought on our behalf; (2) any action asserting a claim of breach of a fiduciary duty or other wrongdoing by any of our directors, officers, employees or agents to us or our stockholders; (3) any action asserting a claim against us arising pursuant to any provision of the General Corporation Law of the State of Delaware or our certificate of incorporation or bylaws; (4) any action to interpret, apply, enforce or determine the validity of our certificate of incorporation or bylaws; or (5) any action asserting a claim governed by the internal affairs doctrine. Our restated certificate of incorporation also provides that any person or entity purchasing or otherwise acquiring any interest in shares of our capital stock will be deemed to have notice of and to have consented to this choice of forum provision. It is possible that a court of law could rule that the choice of forum provision contained in our restated certificate of incorporation is inapplicable or unenforceable if it is challenged in a proceeding or otherwise.

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

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

Transfer Agent and Registrar

The transfer agent and registrar for our common stock will be American Stock Transfer & Trust Company, LLC.

NASDAQ Global Market

We have applied to list our common stock on The NASDAQ Global Market under the symbol “PTGX.”

SHARES ELIGIBLE FOR FUTURE SALE

Immediately prior to this offering, there was no public market for our common stock. Future sales of substantial amounts of common stock in the public market, or the availability of such shares for sale in the public market, could adversely affect market prices prevailing from time to time. As described below, only a limited number of shares will be available for sale shortly after this offering due to contractual and legal restrictions on resale. Nonetheless, sales of our common stock in the public market after such restrictions lapse, or the perception that such sales may occur, could adversely affect the market price of our common stock. Although we have applied to have our common stock listed on The NASDAQ Global Market, we cannot assure you that there will be an active public market for our common stock.

Based on the number of shares of our common stock outstanding as of March 31, 2016 and assuming (1) the issuance of shares in this offering; (2) the conversion of all of outstanding shares of our redeemable convertible preferred stock into an aggregate of 8,439,641 shares of common stock; and (3) no exercise of the underwriters' option to purchase additional shares of common stock, we will have outstanding an aggregate of approximately 14,658,551 shares of common stock.

Of these shares, all shares sold in this offering will be freely tradable without restriction or further registration under the Securities Act, except for any shares purchased by our "affiliates," as that term is defined in Rule 144 under the Securities Act. Shares purchased by our affiliates would be subject to the Rule 144 resale restrictions described below, other than the holding period requirement.

The remaining shares of common stock will be "restricted securities," as that term is defined in Rule 144 under the Securities Act. These restricted securities are eligible for public sale only if they are registered under the Securities Act or if they qualify for an exemption from registration under Rule 144 or 701 under the Securities Act, each of which is summarized below. We expect that substantially all of these shares will be subject to the 180-day lock-up period under the lock-up agreements described below.

In addition, of the 783,341 shares of our common stock that were subject to stock options outstanding as of March 31, 2016, options to purchase 172,236 of such shares of common stock were vested as of such date and, upon exercise, these shares will be eligible for sale subject to the lock–up agreements described below and Rules 144 and 701 under the Securities Act.

Lock-Up Agreements

We, along with our directors, executive officers and substantially all of our other stockholders, optionholders and warrantholders, have agreed with the underwriters, that for a period of 180 days after the date of this prospectus and subject to specified exceptions, we or they will not 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 for the sale of, or otherwise dispose of or transfer any shares of common stock or any securities convertible into or exercisable or exchangeable for shares of common stock, request or demand that we file a registration statement related to our common stock or enter into any swap or other agreement or any transaction that transfers to another, in whole or in part, directly or indirectly, the economic consequence of ownership of any common stock, whether any such swap, agreement or transaction is to be settled by delivery of share of common stock or other securities, in cash or otherwise. Upon expiration of the lock-up period, certain of our stockholders and warrantholders will have the right to require us to register their shares under the Securities Act. See "—Registration Rights" below and "Description of Capital Stock—Registration Rights."

Leerink Partners LLC and Barclays Capital Inc. may, in their sole discretion and at any time or from time to time before the termination of the lock-up period, without public notice, release all or any portion of the securities subject to lock-up agreements. There are no existing agreements between the underwriters and any of our stockholders who will execute a lock-up agreement providing consent to the sale of shares prior to the expiration of the lock-up period.

Upon the expiration of the lock-up period, substantially all of the shares subject to such lock-up restrictions will become eligible for sale, subject to the limitations discussed above.

Rule 144

Affiliate Resales of Restricted Securities—In general, beginning 90 days after the effective date of the registration statement of which this prospectus is a part, a person who is an affiliate of ours, or who was an affiliate at any time during the 90 days before a sale, who has beneficially owned shares of our common stock for at least six months would be entitled to sell in "broker's transactions" or certain "riskless principal transactions" or to market makers, a number of shares within any three-month period that does not exceed the greater of:

- 1% of the number of shares of our common stock then outstanding, which will equal approximately shares immediately after this offering; or
- the average weekly trading volume in our common stock on The NASDAQ Global Market during the four calendar weeks preceding the filing of a notice on Form 144 with respect to such sale.

Affiliate resales under Rule 144 are also subject to the availability of current public information about us. In addition, if the number of shares being sold under Rule 144 by an affiliate during any three-month period exceeds 5,000 shares or has an aggregate sale price in excess of $50,000, the seller must file a notice on Form 144 with the Securities and Exchange Commission and The NASDAQ Global Market concurrently with either the placing of a sale order with the broker or the execution of a sale directly with a market maker.

Non-Affiliate Resales of Restricted Securities—In general, beginning 90 days after the effective date of the registration statement of which this prospectus is a part, a person who is not an affiliate of ours at the time of sale, and has not been an affiliate at any time during the three months preceding a sale, and who has beneficially owned shares of our common stock for at least six months but less than a year, is entitled to sell such shares subject only to the availability of current public information about us. If such person has held our shares for at least one year, such person can resell under Rule 144(b)(1) without regard to any Rule 144 restrictions, including the 90-day public company requirement and the current public information requirement.

Non-affiliate resales are not subject to the manner of sale, volume limitation or notice filing provisions of Rule 144.

Rule 701

In general, under Rule 701, any of an issuer's employees, directors, officers, consultants or advisors who purchases shares from the issuer in connection with a compensatory stock or option plan or other written agreement before the effective date of a registration statement under the Securities Act is entitled to sell such shares 90 days after such effective date in reliance on Rule 144. An affiliate of the issuer can resell shares in reliance on Rule 144 without having to comply with the holding period requirement, and non-affiliates of the issuer can resell shares in reliance on Rule 144 without having to comply with the current public information and holding period requirements.

Equity Plans

We intend to file one or more registration statements on Form S-8 under the Securities Act to register all shares of common stock subject to outstanding stock options and common stock issued or issuable under our equity compensation plans and agreements. We expect to file the registration statement covering shares offered pursuant to these stock plans shortly after the date of this prospectus, permitting the resale of such shares by non-affiliates in the public market without restriction under the Securities Act and the sale by affiliates in the public market subject to compliance with the resale provisions of Rule 144. For a more complete discussion of our compensation plans, see "Executive Compensation—Equity Incentive Award Plans."

Registration Rights

As of March 31, 2016, holders of approximately 8.7 million shares of our common stock, issuable upon conversion of outstanding preferred stock and shares of convertible preferred stock issuable upon exercise of outstanding warrants, or their transferees will be entitled to various rights with respect to the registration of these shares under the Securities Act upon the completion of this offering. Registration of these shares under the Securities Act would result in these shares becoming fully tradable without restriction under the Securities Act immediately upon the effectiveness of the registration, except for shares purchased by affiliates. See "Description of Capital Stock—Registration Rights" for additional information. Shares covered by a registration statement will be eligible for sale in the public market upon the expiration or release from the terms of the lock-up agreement.

MATERIAL U.S. FEDERAL INCOME AND ESTATE TAX CONSIDERATIONS FOR NON-U.S. HOLDERS

The following discussion is a summary of the material U.S. federal income tax consequences to Non-U.S. Holders (as defined below) of the purchase, ownership and disposition of our common stock issued pursuant to this offering, but does not purport to be a complete analysis of all potential tax effects. The effects of other U.S. federal tax laws, except as specifically addressed under "—Estate Tax" below, and any applicable state, local or non-U.S. tax laws are not discussed. This discussion is based on the Code, Treasury regulations promulgated thereunder, judicial decisions, and published rulings and administrative pronouncements of the U.S. Internal Revenue Service (the IRS), in each case in effect as of the date hereof. These authorities may change or be subject to differing interpretations. Any such change or differing interpretation may be applied retroactively in a manner that could adversely affect a Non-U.S. Holder of our common stock. We have not sought and will not seek any rulings from the IRS regarding the matters discussed below. There can be no assurance the IRS or a court will not take a contrary position to that discussed below regarding the tax consequences of the purchase, ownership and disposition of our common stock.

This discussion is limited to Non-U.S. Holders that hold our common stock as a "capital asset" within the meaning of Section 1221 of the Code (generally, property held for investment). This discussion does not address all U.S. federal income tax consequences relevant to a Non-U.S. Holder's particular circumstances, including the impact of the Medicare contribution tax on net investment income. In addition, it does not address consequences relevant to Non-U.S. Holders subject to special rules, including, without limitation:

- U.S. expatriates and former citizens or long-term residents of the United States;
- persons subject to the alternative minimum tax;
- persons holding our common stock as part of a hedge, straddle or other risk reduction strategy or as part of a conversion transaction or other integrated investment;
- banks, insurance companies, and other financial institutions;
- brokers, dealers or traders in securities;
- "controlled foreign corporations," "passive foreign investment companies," and corporations that accumulate earnings to avoid U.S. federal income tax;
- partnerships or other entities or arrangements treated as partnerships for U.S. federal income tax purposes (and investors therein);
- tax-exempt organizations or governmental organizations;
- persons deemed to sell our common stock under the constructive sale provisions of the Code;
- persons who hold or receive our common stock pursuant to the exercise of any employee stock option or otherwise as compensation; and
- tax-qualified retirement plans.

If an entity treated as a partnership for U.S. federal income tax purposes holds our common stock, the tax treatment of a partner in the partnership will depend on the status of the partner, the activities of the partnership and certain determinations made at the partner level. Accordingly, partnerships holding our common stock and the partners in such partnerships should consult their tax advisors regarding the U.S. federal income tax consequences to them.

THIS DISCUSSION IS FOR INFORMATIONAL PURPOSES ONLY AND IS NOT TAX ADVICE. INVESTORS SHOULD CONSULT THEIR TAX ADVISORS WITH RESPECT TO THE

APPLICATION OF THE U.S. FEDERAL INCOME TAX LAWS TO THEIR PARTICULAR SITUATIONS AS WELL AS ANY TAX CONSEQUENCES OF THE PURCHASE, OWNERSHIP AND DISPOSITION OF OUR COMMON STOCK ARISING UNDER THE U.S. FEDERAL ESTATE OR GIFT TAX LAWS OR UNDER THE LAWS OF ANY STATE, LOCAL OR NON-U.S. TAXING JURISDICTION OR UNDER ANY APPLICABLE INCOME TAX TREATY.

Definition of a Non-U.S. Holder

For purposes of this discussion, a "Non-U.S. Holder" is any beneficial owner of our common stock that is neither a "U.S. person" nor an entity treated as a partnership for U.S. federal income tax purposes. A U.S. person is any person that, for U.S. federal income tax purposes, is or is treated as any of the following:

- an individual who is a citizen or resident of the United States;
- a corporation created or organized under the laws of the United States, any state thereof, or the District of Columbia;
- an estate, the income of which is subject to U.S. federal income tax regardless of its source; or
- a trust that (1) is subject to the primary supervision of a U.S. court and the control of one or more "United States persons" (within the meaning of Section 7701(a)(30) of the Code), or (2) has a valid election in effect to be treated as a United States person for U.S. federal income tax purposes.

Distributions

As described in the section entitled "Dividend Policy," we do not anticipate paying any cash dividends in the foreseeable future. However, if we make distributions of cash or property on our common stock, such distributions 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. Amounts not treated as dividends for U.S. federal income tax purposes will constitute a return of capital and will first be applied against and reduce a Non-U.S. Holder's tax basis in our common stock, but not below zero. Any excess will be treated as gain realized on the sale or other disposition of our common stock and will be treated as described under the section of this prospectus titled "—Sale or Other Taxable Disposition" below.

Subject to the discussion below on effectively connected income, dividends (out of earnings and profits) paid to a Non-U.S. Holder of our common stock generally will be subject to U.S. federal withholding tax at a rate of 30% of the gross amount of the dividends, or such lower rate specified by an applicable income tax treaty. To receive the benefit of a reduced treaty rate, a Non-U.S. Holder must furnish to us or the applicable paying agent a valid IRS Form W-8BEN (in the case of an individual), IRS Form W-8BEN-E (in the case of an entity) or applicable successor form, including a U.S. taxpayer identification number and certifying such holder's qualification for the reduced rate. This certification must be provided to us or the applicable paying agent prior to the payment of dividends and must be updated periodically. If the Non-U.S. Holder holds the stock through a financial institution or other agent acting on the Non-U.S. Holder's behalf, the Non-U.S. Holder will be required to provide appropriate documentation to the agent, which then will be required to provide certification to us or our paying agent, either directly or through other intermediaries.

Non-U.S. Holders that do not timely provide the required certification, but that qualify for a reduced treaty rate, may obtain a refund of any excess amounts withheld by timely filing an appropriate claim for refund with the IRS.

If a Non-U.S. Holder holds our common stock in connection with the conduct of a trade or business in the United States, and dividends paid on our common stock are effectively connected with such holder's U.S. trade or business (and are attributable to such holder's permanent establishment in the United States if required by an

applicable tax treaty), the Non-U.S. Holder will be exempt from U.S. federal withholding tax. To claim the exemption, the Non-U.S. Holder must generally furnish a properly executed IRS Form W-8ECI (or applicable successor form).

Any dividends paid on our common stock that are effectively connected with a Non-U.S. Holder's U.S. trade or business (and if required by an applicable income tax treaty, are attributable to a permanent establishment maintained by the Non-U.S. Holder in the United States) generally will be subject to U.S. federal income tax on a net income basis at the regular graduated U.S. federal income tax rates in the same manner as if such holder were a resident of the United States. A Non-U.S. Holder that is a foreign corporation also may be subject to an additional branch profits tax equal to 30% (or such lower rate specified by an applicable income tax treaty) of its effectively connected earnings and profits for the taxable year, as adjusted for certain items. Non-U.S. Holders should consult their tax advisors regarding any applicable income tax treaties that may provide for different rules.

Sale or Other Taxable Disposition

Subject to the discussion below regarding backup withholding and FATCA, a Non-U.S. Holder generally will not be subject to U.S. federal income tax on any gain realized upon the sale or other 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 required by an applicable income tax treaty, is attributable to a permanent establishment maintained by the Non-U.S. Holder in the United States;
- the Non-U.S. Holder is a nonresident alien individual present in the United States for 183 days or more during the taxable year of the disposition, and certain other requirements are met; or
- our common stock constitutes a "United States real property interest" by reason of our status as a United States real property holding corporation (USRPHC), for U.S. federal income tax purposes at any time within the shorter of the five-year period preceding the disposition and the Non-U.S. Holder's holding period for our common stock, and our common stock is not regularly traded on an established securities market during the calendar year in which the sale or other disposition occurs.

The determination of whether we are a USRPHC depends on the fair market value of our U.S. real property interests relative to the fair market value of our other trade or business assets and our foreign real property interests. We believe we are not currently and do not anticipate becoming a USRPHC for U.S. federal income tax purposes.

Gain described in the first bullet point above generally will be subject to U.S. federal income tax on a net income basis at the regular graduated U.S. federal income tax rates in the same manner as if such holder were a resident of the United States. A Non-U.S. Holder that is a foreign corporation may also be subject to an additional branch profits tax equal to 30% (or such lower rate specified by an applicable income tax treaty) of its effectively connected earnings and profits for the taxable year, as adjusted for certain items. Non-U.S. holders should consult their tax advisors regarding any applicable income tax treaties that may provide for different rules.

Gain described in the second bullet point above will be subject to U.S. federal income tax at a flat 30% rate (or such lower rate specified by an applicable income tax treaty), but may be offset by certain U.S.-source capital losses (even though the individual is not considered a resident of the United States), provided that the Non-U.S. Holder has timely filed U.S. federal income tax returns with respect to such losses.

Information Reporting and Backup Withholding

We must report annually to the IRS and to each Non-U.S. Holder the amount of dividends on our common stock paid to such holder and the amount of any tax withheld with respect to those dividends. These information

reporting requirements apply even if no withholding was required because the dividends were effectively connected with the holder's conduct of a U.S. trade or business, or withholding was reduced or eliminated by an applicable income tax treaty. This information also may be made available under a specific treaty or agreement with the tax authorities in the country in which the Non-U.S. Holder resides or is established. Backup withholding, currently at a 28% rate, generally will not apply to payments to a Non-U.S. Holder of dividends on or the gross proceeds of a disposition of our common stock provided the Non-U.S. Holder furnishes the required certification as to its non-U.S. status, such as by providing a valid IRS Form W-8BEN, IRS Form W-8BEN-E or IRS Form W-8ECI, or certain other requirements are met. Notwithstanding the foregoing, backup withholding may apply if the payor has actual knowledge, or reason to know, that the holder is a U.S. person who is not an exempt recipient.

Backup withholding is not an additional tax. If any amount is withheld under the backup withholding rules, the Non-U.S. Holder should consult with a U.S. tax advisor regarding the possibility of and procedure for obtaining a refund or a credit against the Non-U.S. Holder's U.S. federal income tax liability, if any.

Additional Withholding Tax on Payments Made to Foreign Accounts

Sections 1471 through 1474 of the Code (commonly referred to as FATCA) will impose a U.S. federal withholding tax of 30% on certain payments, including dividends on and the gross proceeds of a disposition of our common stock, made to a "foreign financial institution" (as specially defined under these rules) unless such institution enters into an agreement with the U.S. government to withhold on certain payments and to collect and provide to the U.S. tax authorities substantial information regarding U.S. account holders of such institution (which includes certain equity and debt holders of such institution, as well as certain account holders that are foreign entities with U.S. owners) or an exemption applies. FATCA also generally will impose a U.S. federal withholding tax of 30% on certain payments, including dividends on and the gross proceeds of a disposition of our common stock, made to a non-financial foreign entity unless such entity provides the withholding agent a certification identifying the direct and indirect U.S. owners of the entity or an exemption applies. An intergovernmental agreement between the United States and an applicable foreign country may modify these requirements. Under certain circumstances, a Non-U.S. Holder might be eligible for refunds or credits of such taxes. These withholding taxes currently may be imposed on dividends paid on our common stock. These withholding taxes may also be imposed on gross proceeds from sales or other dispositions of our common stock after December 31, 2018.

Prospective investors should consult their tax advisors regarding the potential application of withholding under FATCA to their investment in our common stock.

Estate Tax

Individuals who are Non-U.S. Holders (as specially defined for U.S. federal estate tax purposes) whose property is potentially includible in such an individual's gross estate for U.S. federal estate tax purposes (for example, a trust funded by such an individual and with respect to which the individual has retained certain interests or powers), should note that, absent an applicable treaty benefit, our common stock generally will be treated as U.S. situs property subject to U.S. federal estate tax.

UNDERWRITING

Leerink Partners LLC and Barclays Capital Inc. are acting as representatives of each of the underwriters named below. Subject to the terms and conditions set forth in an underwriting agreement among us and the underwriters, we have agreed to sell to the underwriters, and each of the underwriters has agreed, severally and not jointly, to purchase from us, the number of shares of common stock set forth opposite its name below.

Underwriter	Number of Shares
Leerink Partners LLC	
Barclays Capital Inc.	
BMO Capital Markets Corp.	
Total	5,835,000

Subject to the terms and conditions set forth in the underwriting agreement, the underwriters have agreed, severally and not jointly, to purchase all of the shares sold under the underwriting agreement if any of these shares are purchased, other than those shares covered by the option described below. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the non-defaulting underwriters may be increased or the underwriting agreement may be terminated.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act, or to contribute to payments the underwriters may be required to make in respect of those liabilities.

The underwriters are offering the shares, subject to prior sale, when, as and if issued to and accepted by them, subject to approval of legal matters by their counsel, including the validity of the shares, and other conditions contained in the underwriting agreement, such as the receipt by the underwriters of officers' certificates and legal opinions. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Commissions and Discounts

The representatives have advised us that the underwriters propose initially to offer the shares to the public at the public offering price set forth on the cover of this prospectus and to dealers at that price less a concession not in excess of per share. After the initial offering, the public offering price, concession or any other term of the offering may be changed.

The following table shows the public offering price, underwriting discount and proceeds before expenses to us. The information assumes either no exercise or full exercise by the underwriters of their option to purchase additional shares of our common stock.

	Per Share	Without Option	With Option
Public offering price	$	$	$
Underwriting discount	$	$	$
Proceeds, before expenses, to us	$	$	$

We estimate expenses payable by us in connection with this offering, other than the underwriting discounts and commissions referred to above, will be approximately . We also have agreed to reimburse the underwriters for up to for their FINRA counsel fee. In accordance with FINRA Rule 5110, this reimbursed fee is deemed underwriting compensation for this offering.

Certain of our existing stockholders and their affiliated entities, including investors affiliated with certain of our directors, have indicated an interest in purchasing an aggregate of up to approximately $40.0 million in shares of our common stock in this offering at the initial public offering price and on the same terms as the other

purchasers in this offering. However, because indications of interest are not binding agreements or commitments to purchase, these investors may determine to purchase fewer shares than they indicate an interest in purchasing or not to purchase any shares in this offering. It is also possible that these investors could indicate an interest in purchasing more shares of our common stock. In addition, the underwriters could determine to sell fewer shares to any of these investors than the investors indicate an interest in purchasing or not to sell any shares to these investors. Whether or not these investors purchase any or all of the shares for which they indicated an interest in purchasing will not affect the underwriters' commitment to purchase the common shares offered by us if the underwriters purchase any shares.

Option to Purchase Additional Shares

We have granted an option to the underwriters, exercisable for 30 days after the date of this prospectus, to purchase up to additional shares at the public offering price, less the underwriting discount. If the underwriters exercise this option, each will be obligated, subject to conditions contained in the underwriting agreement, to purchase a number of additional shares proportionate to that underwriter's initial amount reflected in the above table.

No Sales of Similar Securities

We, our executive officers and directors and all of our other existing security holders have agreed, subject to certain exceptions, not to sell or transfer any common stock or securities convertible into or exchangeable or exercisable for common stock, for 180 days after the date of this prospectus without first obtaining the written consent of Leerink Partners LLC and Barclays Capital Inc. Specifically, we and these other persons have agreed, with certain limited exceptions, not to directly or indirectly:

- offer, pledge, sell or contract to sell any common stock;
- sell any option or contract to purchase any common stock;
- purchase any option or contract to sell any common stock;
- grant any option, right or warrant for the sale of any common stock;
- otherwise dispose of or transfer any common stock;
- request or demand that we file a registration statement related to the common stock; or
- enter into any swap or other agreement or any transaction that transfers, in whole or in part, directly or indirectly, the economic consequence of ownership of any common stock, whether any such swap, agreement or transaction is to be settled by delivery of shares of common stock or other securities, in cash or otherwise.

This lock-up provision applies to common stock and to securities convertible into or exchangeable or exercisable for common stock. It also applies to common stock owned now or acquired later by the person executing the agreement or for which the person executing the agreement later acquires the power of disposition.

The restrictions described in the preceding paragraphs do not apply to:

- transfers or dispositions of shares of common stock (or any security convertible into or exercisable or exchangeable for common stock):
    - as a bona fide gift or gifts;
    - to the immediate family of or any trust for the direct or indirect benefit of the person subject to the lock-up restrictions; or
    - if the person subject to the lock-up restriction is an entity, as a distribution to the limited partners or stockholders of the such entity; or

- to a corporation, partnership, limited liability company, investment fund or other entity that controls or is controlled by, or is under common control with, the person subject to the lock-up restrictions, or, in the case of an investment fund, that is managed by, or is under common management with, the person subject to the lock-up restrictions (including a fund managed by the same manager or managing member or general partner or management company or by an entity controlling, controlled by, or under common control with such manager or managing member or general partner or management company as the person subject to the lock-up restrictions or who shares a common investment advisor with the person subject to the lock-up restrictions); or *provided* that in the case of any transfer or distribution pursuant to the above, (i) each donee, trustee, distributee or transferee shall sign and deliver to the representatives a lock-up letter substantially in the form executed by the party subject to the lock up restrictions, (ii) such transfer shall not involve a disposition for value, (iii) such transfers are not required to be reported with the Securities and Exchange Commission in accordance with Section 16 of the Exchange Act, and (iv) the person subject to the lock-up restriction does not voluntarily effect any public filing or report regarding such transfers (other than certain required filings after the expiration of the lock-up restrictions).
- sales or transfers to the underwriters in this offering; or
- transfers to the company upon a vesting event of the company's securities or upon the exercise or conversion of options or warrants to purchase the company's securities, in each case, on a "cashless" or "net exercise" basis in connection with such vesting or exercise, *provided* that (i) such transfers are not required to be reported with the Securities and Exchange Commission in accordance with Section 16 of the Exchange Act and (ii) the person subject to such lock-up restrictions does not otherwise voluntarily effect any public filing or report regarding such transfers during the lock-up period; or
- the conversion of shares of preferred stock of the company into shares of common stock or exercise of preferred stock warrants that would expire or terminate in connection with this offering *provided* that any shares of capital stock received upon any such conversion or exercise remain subject to the terms of the lock-up letter; or
- transfers by operation of law, including pursuant to a domestic order or a negotiated divorce settlement, provided that the common stock or other securities received upon such transfer remain subject to the terms of the lock-up letter; or
- transfers to the company in connection with the termination of the employment or other service with the company of the person subject to the lock-up restrictions, *provided* that any filing made pursuant to Section 16 of the Exchange Act clearly indicate that the filing relate to the circumstances described in this paragraph; or
- transfers pursuant to a bona fide third party tender offer, merger, consolidation or other similar transaction made to all holders of common stock or other securities subject to the lock-up and involving a Change of Control (defined below) of the company, provided that in the event that the tender offer, merger, consolidation or other such transaction is not completed, the common stock or other securities subject to the lock-up which are owned by the person subject to the lock-up restrictions shall remain subject to the restrictions contained in the lock-up letter. "Change of Control" under the lock-up letter means the transfer (whether by tender offer, merger, consolidation or other similar transaction), in one transaction or a series of related transactions, to a person or group of affiliated persons (other than an underwriter pursuant to this offering), of the company's voting securities if, after such transfer, such person or group of affiliated persons would hold more than 50% of the outstanding voting securities of the company (or the surviving entity); or
- sales of shares of common stock acquired in open market transactions after the completion of this offering of the shares, *provided* such sales are not required during the 180-day period to be reported

in any press release or public report or filing with SEC or otherwise (other than certain required filings after the expiration of the 180 day period) and the person subject to the lock-up restriction does not otherwise voluntarily effect any press release, public filing or report regarding such sales during the 180-day period; or

- the exercise any rights to purchase, exchange or convert any stock options granted pursuant to the company's equity incentive plans existing as of the date of the underwriting agreement or warrants or any other securities existing as of the date of the underwriting agreement, which securities are convertible into or exchangeable or exercisable for common stock, if and only if (x) the shares of common stock received upon such exercise, purchase, exchange or conversion shall remain subject to the terms of the lock-up letter agreement, (y) such exercise, exchange or conversion is not required during the 180 day period to be reported in any press release or public report or filing with the SEC (including, without limitation, any filing under Section 16 of the Exchange Act), or otherwise and (z) the undersigned does not otherwise voluntarily effect any public filing or report regarding such transfers during the 180 day period.

NASDAQ Global Market Listing

We have applied to list our common stock on The NASDAQ Global Market, subject to notice of issuance, under the symbol "PTGX."

Before this offering, there has been no public market for our common stock. The initial public offering price will be determined through negotiations between us and the representatives. In addition to prevailing market conditions, the factors to be considered in determining the initial public offering price are:

- the valuation multiples of publicly traded companies that the representatives believe to be comparable to us;
- our financial information;
- the history of, and the prospects for, our company and the industry in which we compete;
- an assessment of our management, its past and present operations, and the prospects for, and timing of, our future revenues;
- the present state of our development; and
- the above factors in relation to market values and various valuation measures of other companies engaged in activities similar to ours.

An active trading market for the shares may not develop. It is also possible that after the offering the shares will not trade in the public market at or above the initial public offering price.

The underwriters do not expect to sell more than 5% of the shares in the aggregate to accounts over which they exercise discretionary authority.

Price Stabilization, Short Positions and Penalty Bids

Until the distribution of the shares is completed, SEC rules may limit underwriters and selling group members from bidding for and purchasing our common stock. However, the representatives may engage in transactions that stabilize the price of the common stock, such as bids or purchases to peg, fix or maintain that price.

In connection with the offering, the underwriters may purchase and sell our common stock in the open market. These transactions may include short sales, purchases on the open market to cover positions created by short sales and stabilizing transactions. Short sales involve the sale by the underwriters of a greater number of

shares than they are required to purchase in the offering. "Covered" short sales are sales made in an amount not greater than the underwriters' option to purchase additional shares described above. The underwriters may close out any covered short position by either exercising their option to purchase additional shares or purchasing shares in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the option granted to them. "Naked" short sales are sales in excess of such option. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of our common stock in the open market after pricing that could adversely affect investors who purchase in the offering. Stabilizing transactions consist of various bids for or purchases of shares of common stock made by the underwriters in the open market prior to the closing of the offering.

The underwriters may also impose a penalty bid. This occurs when a particular underwriter repays to the representatives a portion of the underwriting discount received by it because the representatives have repurchased shares sold by or for the account of such underwriter in stabilizing or short covering transactions.

Similar to other purchase transactions, the underwriters' purchases to cover syndicate short sales may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market. The underwriters may conduct these transactions on The NASDAQ Global Market, in the over-the-counter market or otherwise.

Neither we nor any of the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our common stock. In addition, neither we nor any of the underwriters make any representation that the representatives will engage in these transactions or that these transactions, once commenced, will not be discontinued without notice.

Electronic Distribution

In connection with the offering, certain of the underwriters or securities dealers may distribute prospectuses by electronic means, such as e-mail.

Other Relationships

Some of the underwriters and their affiliates have engaged in and may in the future engage in, investment banking and other commercial dealings in the ordinary course of business with us or our affiliates. They have received, or may in the future receive customary fees and commissions for these transactions.

In addition, in the ordinary course of their business activities, the underwriters and their affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers.

Such investments and securities activities may involve securities and/or instruments of ours or our affiliates. The underwriters and their affiliates may also make investment recommendations and/or publish or express independent research views in respect of such securities or financial instruments and may hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

Notice to Prospective Investors in the European Economic Area

In relation to each Member State of the European Economic Area (each, a "Relevant Member State"), no offer of shares may be made to the public in that Relevant Member State other than:

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

(b) to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the representatives; or

(c) in any other circumstances falling within Article 3(2) of the Prospectus Directive, provided that no such offer of shares shall require the Company or the representatives to publish a prospectus pursuant to Article 3 of the Prospectus Directive or supplement a prospectus pursuant to Article 16 of the Prospectus Directive.

Each person in a Relevant Member State who initially acquires any shares or to whom any offer is made will be deemed to have represented, acknowledged and agreed that it is a "qualified investor" within the meaning of the law in that Relevant Member State implementing Article 2(1)(e) of the Prospectus Directive. In the case of any shares being offered to a financial intermediary as that term is used in Article 3(2) of the Prospectus Directive, each such financial intermediary will be deemed to have represented, acknowledged and agreed that the shares acquired by it in the offer have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in circumstances which may give rise to an offer of any shares to the public other than their offer or resale in a Relevant Member State to qualified investors as so defined or in circumstances in which the prior consent of the representatives has been obtained to each such proposed offer or resale.

The company, the representatives and their affiliates will rely upon the truth and accuracy of the foregoing representations, acknowledgements and agreements.

This prospectus has been prepared on the basis that any offer of shares in any Relevant Member State will be made pursuant to an exemption under the Prospectus Directive from the requirement to publish a prospectus for offers of shares. Accordingly any person making or intending to make an offer in that Relevant Member State of shares which are the subject of the offering contemplated in this prospectus may only do so in circumstances in which no obligation arises for the company or any of the underwriters to publish a prospectus pursuant to Article 3 of the Prospectus Directive in relation to such offer. Neither the company nor the underwriters have authorized, nor do they authorize, the making of any offer of shares in circumstances in which an obligation arises for the company or the underwriters to publish a prospectus for such offer.

For the purpose of the above provisions, the expression "an offer to the public" in relation to any 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 the shares to be offered so as to enable an investor to decide to purchase or subscribe the shares, as the same may be varied in the Relevant Member State by any measure implementing the Prospectus Directive in the Relevant Member State and the expression "Prospectus Directive" means Directive 2003/71/EC (including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member States) and includes any relevant implementing measure in the Relevant Member State and the expression "2010 PD Amending Directive" means Directive 2010/73/EU.

Notice to Prospective Investors in the United Kingdom

In addition, in the United Kingdom, this document is being distributed only to, and is directed only at, and any offer subsequently made may only be directed at persons who are "qualified investors" (as defined in the Prospectus 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"). This document must not be acted on or relied on in the United Kingdom by persons who are not relevant persons. In the United Kingdom, any investment or investment activity to which this document relates is only available to, and will be engaged in with, relevant persons.

Notice to Prospective Investors in Switzerland

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

Neither this document nor any other offering or marketing material relating to the offering, the company or the shares have been or will be filed with or approved by any Swiss regulatory authority. In particular, this document will not be filed with, and the offer of shares will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA (FINMA), and the offer of shares has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes (CISA). The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of shares.

Notice to Prospective Investors in the Dubai International Financial Centre

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

Notice to Prospective Investors in 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 the offering. This 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 required for a prospectus, product disclosure statement or other disclosure document under the Corporations Act.

Any offer in Australia of the 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 the shares without disclosure to investors under Chapter 6D of the Corporations Act.

The 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 the 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 shares must observe such Australian on-sale restrictions.

This prospectus contains 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 is appropriate to their needs, objectives and circumstances, and, if necessary, seek expert advice on those matters.

Notice to Prospective Investors in Hong Kong

The shares have not been offered or sold and will not be offered or sold in Hong Kong, by means of any document, other than (a) to "professional investors" as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance; or (b) in other circumstances which do not result in the document being a "prospectus" as defined in the Companies Ordinance (Cap. 32) of Hong Kong or which do not constitute an offer to the public within the meaning of that Ordinance. No advertisement, invitation or document relating to the shares has been or may be issued or has been or may be in the possession of any person for the purposes of issue, whether in Hong Kong or elsewhere, which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted to do so under the securities laws of Hong Kong) other than with respect to shares which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" as defined in the Securities and Futures Ordinance and any rules made under that Ordinance.

Notice to Prospective Investors in Japan

The shares have not been and will not be registered under the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948, as amended) and, accordingly, will not be offered or sold, directly or indirectly, in Japan, or for the benefit of any Japanese Person or to others for re-offering or resale, directly or indirectly, in Japan or to any Japanese Person, except in compliance with all applicable laws, regulations and ministerial guidelines promulgated by relevant Japanese governmental or regulatory authorities in effect at the relevant time. For the purposes of this paragraph, "Japanese Person" shall mean any person resident in Japan, including any corporation or other entity organized under the laws of Japan.

Notice to Prospective Investors in Singapore

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of shares may not be circulated or distributed, nor may the shares be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore (the SFA), (ii) to a relevant person pursuant to Section 275(1), or any person pursuant to Section 275(1A), and in accordance with the conditions specified in Section 275, of the SFA, or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the shares are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

(a) a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or

(b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor,

securities (as defined in Section 239(1) of the SFA) of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the shares pursuant to an offer made under Section 275 of the SFA except:

(c) to an institutional investor or to a relevant person defined in Section 275(2) of the SFA, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA;

(d) where no consideration is or will be given for the transfer;

(e) where the transfer is by operation of law;

(f) as specified in Section 276(7) of the SFA; or

(g) as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore.

Notice to Prospective Investors in Canada

This document constitutes an "exempt offering document" as defined in and for the purposes of applicable Canadian securities laws. No prospectus has been filed with any securities commission or similar regulatory authority in Canada in connection with the offer and sale of the securities described herein (the "Securities"). No securities commission or similar regulatory authority in Canada has reviewed or in any way passed upon this document or on the merits of the Securities and any representation to the contrary is an offence.

Canadian investors are advised that this document has been prepared in reliance on section 3A.3 of National Instrument 33-105 *Underwriting Conflicts* ("NI 33-105"). Pursuant to section 3A.3 of NI 33-105, this document is exempt from the requirement to provide investors with certain conflicts of interest disclosure pertaining to "connected issuer" and/or "related issuer" relationships as would otherwise be required pursuant to subsection 2.1(1) of NI 33-105.

Resale Restrictions

The offer and sale of the Securities in Canada is being made on a private placement basis only and is exempt from the requirement to prepare and file a prospectus under applicable Canadian securities laws. Any resale of Securities acquired by a Canadian investor in this offering must be made in accordance with applicable Canadian securities laws, which may vary depending on the relevant jurisdiction, and which may require resales to be made in accordance with Canadian prospectus requirements, a statutory exemption from the prospectus requirements, in a transaction exempt from the prospectus requirements or otherwise under a discretionary exemption from the prospectus requirements granted by the applicable local Canadian securities regulatory authority. These resale restrictions may under certain circumstances apply to resales of the Securities outside of Canada.

Representations of Purchasers

Each Canadian investor who purchases the Securities will be deemed to have represented to the issuer and to each dealer from whom a purchase confirmation is received, as applicable, that the investor (i) is purchasing as principal, or is deemed to be purchasing as principal in accordance with applicable Canadian securities laws, for investment only and not with a view to resale or redistribution; (ii) is an "accredited investor" as such term is defined in section 1.1 of National Instrument 45-106 *Prospectus Exemptions* ("NI 45-106") or, in Ontario, as such term is defined in section 73.3(1) of the *Securities Act* (Ontario); and (iii) is a "permitted client" as such term is defined in section 1.1 of National Instrument 31-103 *Registration Requirements, Exemptions and Ongoing Registrant Obligations*.

Taxation and Eligibility for Investment

Any discussion of taxation and related matters contained in this document does not purport to be a comprehensive description of all of the tax considerations that may be relevant to a Canadian investor when deciding to purchase the Securities and, in particular, does not address any Canadian tax considerations. No representation or warranty is hereby made as to the tax consequences to a resident, or deemed resident, of Canada of an investment in the Securities or with respect to the eligibility of the Securities for investment by such investor under relevant Canadian federal and provincial legislation and regulations.

Rights of Action for Damages or Rescission

Securities legislation in certain of the Canadian jurisdictions provides certain purchasers of securities pursuant to an offering memorandum, including where the distribution involves an "eligible foreign security" as such term is defined in Ontario Securities Commission Rule 45-501 *Ontario Prospectus and Registration Exemptions* and in Multilateral Instrument 45-107 *Listing Representation and Statutory Rights of Action Disclosure Exemptions*, as applicable, with a remedy for damages or rescission, or both, in addition to any other rights they may have at law, where the offering memorandum, or other offering document that constitutes an offering memorandum, and any amendment thereto, contains a "misrepresentation" as defined under applicable Canadian securities laws. These remedies, or notice with respect to these remedies, must be exercised or delivered, as the case may be, by the purchaser within the time limits prescribed under, and are subject to limitations and defences under, applicable Canadian securities legislation. In addition, these remedies are in addition to and without derogation from any other right or remedy available at law to the investor.

Language of Documents

Upon receipt of this document, each Canadian investor hereby confirms that it has expressly requested that all documents evidencing or relating in any way to the sale of the Securities described herein (including for greater certainty any purchase confirmation or any notice) be drawn up in the English language only. *Par la réception de ce document, chaque investisseur canadien confirme par les présentes qu'il a expressément exigé que tous les documents faisant foi ou se rapportant de quelque manière que ce soit à la vente des valeurs mobilières décrites aux présentes (incluant, pour plus de certitude, toute confirmation d'achat ou tout avis) soient rédigés en anglais seulement.*

LEGAL MATTERS

The validity of the shares of common stock being offered by this prospectus will be passed upon for us by Cooley LLP, Palo Alto, California. The underwriters are being represented by Latham & Watkins LLP, Menlo Park, California.

EXPERTS

The consolidated financial statements as of December 31, 2014 and 2015 and for the years then ended included in this prospectus have been so included in reliance on the report (which contains an explanatory paragraph relating to the Company's liquidity position) of PricewaterhouseCoopers LLP, an independent registered public accounting firm, given on the authority of said firm as experts in auditing and accounting.

WHERE YOU CAN FIND ADDITIONAL INFORMATION

We have filed with the SEC a registration statement on Form S-1, including exhibits and schedules, under the Securities Act, with respect to the shares of common stock being offered by this prospectus. This prospectus, which constitutes part of the registration statement, does not contain all of the information in the registration statement and its exhibits. For further information with respect to us and the common stock offered by this prospectus, we refer you to the registration statement and its exhibits. Statements contained in this prospectus as to the contents of any contract or any other document referred to are not necessarily complete, and in each instance, we refer you to the copy of the contract or other document filed as an exhibit to the registration statement. Each of these statements is qualified in all respects by this reference.

You can read our SEC filings, including the registration statement, over the Internet at the SEC's website at www.sec.gov. You may also read and copy any document we file with the SEC at its public reference facilities at 100 F Street, NE, Washington, D.C. 20549. You may also obtain copies of these documents at prescribed rates by writing to the Public Reference Section of the SEC at 100 F Street, NE, Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the public reference facilities.

Upon the completion of this offering, we will be subject to the information reporting requirements of the Securities Exchange Act of 1934 and we will file reports, proxy statements and other information with the SEC. These reports, proxy statements and other information will be available for inspection and copying at the public reference room and web site of the SEC referred to above. We also maintain a website at www.protagonist-inc.com, at which, following the completion of this offering, you may access these materials free of charge as soon as reasonably practicable after they are electronically filed with, or furnished to, the SEC. Information contained on or accessible through our website is not a part of this prospectus, and the inclusion of our website address in this prospectus is an inactive textual reference only.

PROTAGONIST THERAPEUTICS, INC.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Years Ended December 31, 2014 and 2015 and Three Months Ended March 31, 2015 and 2016

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Board of Directors and Stockholders of
Protagonist Therapeutics, Inc.

In our opinion, the accompanying consolidated balance sheets and the related consolidated statements of operations, comprehensive loss, redeemable convertible preferred stock and stockholders' deficit, and of cash flows present fairly, in all material respects, the financial position of Protagonist Therapeutics, Inc. and its subsidiary ("the Company") at December 31, 2015 and 2014, and the results of its operations and its cash flows for the years then ended in conformity with accounting principles generally accepted in the United States of America. These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits. We conducted our audits of these statements in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

As discussed in Note 1 to the consolidated financial statements, the Company has incurred substantial recurring losses and negative cash flows from operations. Management's plans with respect to its liquidity are also discussed in Note 1.

/s/ PricewaterhouseCoopers LLP

San Jose, California
May 3, 2016, except for the effects of additional disclosures relating to the Company's liquidity position described in Note 1, as to which the date is July 11, 2016, and for the effects of the reverse stock split described in the second to the last paragraph of Note 16, as to which the date is August 1, 2016.

PROTAGONIST THERAPEUTICS, INC.

Consolidated Balance Sheets

(In thousands, except share data)

	December 31, 2014	December 31, 2015
Assets		
Current assets:		
Cash and cash equivalents	$ 9,324	$ 4,055
Restricted cash	10	10
Available-for-sale securities	—	7,868
Research and development tax incentive receivable	523	715
Prepaid expenses and other current assets	56	1,558
Total current assets	9,913	14,206
Property and equipment, net	415	609
Other assets	—	30
Total assets	$10,328	$ 14,845
Liabilities, Redeemable Convertible Preferred Stock and Stockholders' Deficit		
Current liabilities:		
Accounts payable	$ 349	$ 1,247
Accrued expenses and other payables	1,001	1,879
Total current liabilities	1,350	3,126
Redeemable convertible preferred stock tranche liability	—	1,643
Redeemable convertible preferred stock warrant liability	1,023	480
Total liabilities	2,373	5,249
Commitments and contingencies (Note 6)		
Redeemable convertible preferred stock, $0.00001 par value: 51,231,041 and 126,374,911 shares authorized as of December 31, 2014 and 2015; 42,037,500 and 77,185,117 shares issued and outstanding as of December 31, 2014 and 2015; redemption value of $41,538 as of December 31, 2015	20,576	36,996
Stockholders' deficit:		
Common stock, $0.00001 par value, 70,000,000 and 160,000,000 shares authorized as of December 31, 2014 and 2015; 228,557 and 272,409 shares issued and outstanding as of December 31, 2014 and 2015	—	—
Additional paid-in capital	37	118
Accumulated other comprehensive loss	(100)	(102)
Accumulated deficit	(12,558)	(27,416)
Total stockholders' deficit	(12,621)	(27,400)
Total liabilities, redeemable convertible preferred stock and stockholders' deficit	$10,328	$ 14,845

The accompanying notes are an integral part of these consolidated financial statements.

PROTAGONIST THERAPEUTICS, INC.

Consolidated Statements of Operations

(In thousands, except share and per share data)

	Year Ended December 31,	
	2014	2015
Operating expenses:		
Research and development	$ 7,459	$ 11,831
General and administrative	1,860	2,963
Total operating expenses	9,319	14,794
Loss from operations	(9,319)	(14,794)
Interest income	16	19
Change in fair value of redeemable convertible preferred stock tranche and warrant liabilities	(1,769)	(83)
Net loss	$ (11,072)	$ (14,858)
Net loss attributable to common stockholders	$ (11,218)	$ (14,933)
Net loss per share attributable to common stockholders, basic and diluted	$ (49.38)	$ (59.32)
Weighted-average shares used to compute net loss per share attributable to common stockholders, basic and diluted	227,197	251,717
Pro forma net loss per share attributable to common stockholders, basic and diluted (unaudited)		$ (3.57)
Pro forma weighted-average shares used to compute net loss per share attributable to common stockholders, basic and diluted (unaudited)		4,313,032

The accompanying notes are an integral part of these consolidated financial statements.

PROTAGONIST THERAPEUTICS, INC.

Consolidated Statements of Comprehensive Loss

(In thousands)

	Year Ended December 31,	
	2014	2015
Net loss	$(11,072)	$(14,858)
Other comprehensive loss:		
Gain (loss) on translation of foreign operations, net of tax	(54)	3
Unrealized loss on available-for-sale securities	—	(5)
Comprehensive loss	$(11,126)	$(14,860)

The accompanying notes are an integral part of these consolidated financial statements.

PROTAGONIST THERAPEUTICS, INC.

Consolidated Statements of Redeemable Convertible Preferred Stock and Stockholders' Deficit

(In thousands, except share and per share data)

	Redeemable Convertible Preferred Stock		Common Stock		Additional Paid-In Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Deficit
	Shares	Amount	Shares	Amount				
Balance at December 31, 2013	24,037,500	$ 9,122	226,009	$—	$ 135	$ (46)	$ (1,483)	$ (1,394)
Issuance of Series B redeemable convertible preferred stock	18,000,000	9,000	—	—	—	—	—	—
Settlement of fair value of Series B redeemable convertible preferred stock tranche liability	—	2,308	—	—	—	—	—	—
Accretion of redeemable convertible preferred stock to redemption value	—	146	—	—	(143)	—	(3)	(146)
Stock-based compensation expense	—	—	—	—	42	—	—	42
Issuance of common stock upon the exercise of options	—	—	2,548	—	3	—	—	3
Other comprehensive loss	—	—	—	—	—	(54)	—	(54)
Net loss	—	—	—	—	—	—	(11,072)	(11,072)
Balance at December 31, 2014	42,037,500	20,576	228,557	—	37	(100)	(12,558)	(12,621)
Issuance of Series C redeemable convertible preferred stock, net of issuance costs of $138 and reclassification of $1,017 to redeemable convertible preferred stock tranche liability	35,147,617	16,345	—	—	—	—	—	—
Accretion of redeemable convertible preferred stock to redemption value	—	75	—	—	(75)	—	—	(75)
Stock-based compensation expense	—	—	—	—	99	—	—	99
Issuance of common stock upon the exercise of options	—	—	43,852	—	57	—	—	57
Other comprehensive loss	—	—	—	—	—	(2)	—	(2)
Net loss	—	—	—	—	—	—	(14,858)	(14,858)
Balance at December 31, 2015	77,185,117	$36,996	272,409	$—	$ 118	$(102)	$(27,416)	$(27,400)

The accompanying notes are an integral part of these consolidated financial statements.

PROTAGONIST THERAPEUTICS, INC.

Consolidated Statements of Cash Flows

(In thousands)

	Year Ended December 31,	
	2014	**2015**
CASH FLOWS FROM OPERATING ACTITIVIES		
Net loss	$(11,072)	$(14,858)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	258	247
Amortization of premium on available-for-sale securities	—	(8)
Stock-based compensation	42	99
Change in fair value associated with redeemable convertible preferred stock tranche liability	897	626
Change in fair value of redeemable convertible preferred stock warrant liability	872	(543)
Changes in operating assets and liabilities:		
Research and development tax credit receivable	259	(192)
Prepaid expenses and other current assets	604	(1,502)
Other assets	—	(30)
Accounts payable	179	898
Accrued expenses and other payables	218	878
Net cash used in operating activities	(7,743)	(14,385)
CASH FLOWS FROM INVESTING ACTIVITIES		
Purchase of available-for-sale securities	—	(7,865)
Purchase of property and equipment	(299)	(399)
Net cash used in investing activities	(299)	(8,264)
CASH FLOWS FROM FINANCING ACTIVITIES		
Proceeds from issuance of redeemable convertible preferred stock, net of issuance costs	9,000	17,362
Proceeds from issuance of common stock upon exercise of stock options	3	57
Net cash provided by financing activities	9,003	17,419
Effect on exchange rate changes on cash and cash equivalents	(97)	(39)
Net increase (decrease) in cash and cash equivalents	864	(5,269)
Cash and cash equivalents, beginning of period	8,460	9,324
Cash and cash equivalents, end of period	$ 9,324	$ 4,055
SUPPLEMENTAL DISCLOSURES OF NON-CASH FINANCING INFORMATION:		
Settlement of fair value of redeemable convertible preferred stock liability	$ 2,308	$ —
Tranche liability in connection with the Series C redeemable convertible preferred stock financing	$ —	$ 1,017
Accretion of redeemable convertible preferred stock	$ 146	$ 75

The accompanying notes are an integral part of these consolidated financial statements.

1. Organization and Description of Business

Protagonist Therapeutics, Inc. (the Company) was incorporated in the state of Delaware on August 22, 2006 and is headquartered in Milpitas, California. The Company is a clinical-stage biopharmaceutical company with a proprietary peptide-based technology platform focused on discovering and developing new chemical entities to address significant unmet medical needs.

Protagonist Pty Ltd is a wholly-owned subsidiary located in Brisbane, Australia. The Company manages its operations as a single operating segment.

Need for Additional Capital

In the course of its development activities, the Company has sustained operating losses and expects such losses to continue over the next several years. The Company's ultimate success depends on the outcome of its research and development activities such that over the long term it can receive approval to launch products that will generate sufficient revenue to cover its expenses. The Company has funded its operations to date primarily through the sale of convertible preferred stock. As of December 31, 2015, the Company had an accumulated deficit of $27.4 million. Management expects to incur additional losses in the future to conduct product research and development and will need to raise additional capital to fully implement its business plan. The Company intends to raise such capital through the issuance of additional equity. However, if such financing is not available at adequate levels and on terms that are acceptable to the Company, the Company will need to reevaluate its operating plans. Management believes that its cash, cash equivalents and available-for-sale securities of $11.9 million as of December 31, 2015, and the net proceeds of approximately $22.5 million from the closing of its Series C Second Tranche redeemable convertible preferred stock financing in March 2016 will be sufficient to fund the Company's operating requirements through at least December 31, 2016.

2. Summary of Significant Accounting Policies

Basis of Presentation and Consolidation

The accompanying consolidated financial statements include the accounts of the Company and its wholly owned subsidiary, Protagonist Pty Ltd and have been prepared in conformity with accounting principles generally accepted in the United States of America (U.S. GAAP). All intercompany balances and transactions have been eliminated in consolidation.

The financial statements of Protagonist Pty Ltd use the Australian dollar as the functional currency since the majority of expense transactions occur in such currency. Gains and losses from foreign currency transactions were not material for all periods presented. The re-measurement from Australian dollar to U.S. dollars is outlined below:

a. Equity accounts, except for the change in retained earnings during the year, have been translated using historical exchange rates.

b. All other Australian dollar denominated assets and liabilities as of December 31, 2014 and 2015 have been translated using the year-end exchange rate.

c. The consolidated statements of operations have been translated at the weighted average exchange rates in effect during each year, except for depreciation, which has been translated at historical exchange rates.

2. Summary of Significant Accounting Policies (Continued)

d. Foreign currency translation gains and losses are reported as a component of Stockholder's deficit in accumulated other comprehensive loss on the consolidated balance sheets.

Use of Estimates

The preparation of the financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities as of the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. On an ongoing basis, management evaluates its estimates, including those related to accruals for research and development activities, fair value of redeemable convertible preferred stock tranche liability, fair value of redeemable convertible preferred stock warrant liability, fair value of common stock, stock-based compensation and income taxes. Management bases these estimates on historical and anticipated results, trends, and various other assumptions that the Company believes are reasonable under the circumstances, including assumptions as to future events. Actual results may differ from those estimates.

Concentrations of Credit Risk

Financial instruments that potentially subject the Company to a concentration of credit risk consist of cash, cash equivalents and available-for-sale securities. Substantially all the Company's cash is held by one financial institution that management believes is of high credit quality. Such deposits may, at times, exceed federally insured limits.

Cash Equivalents

Cash equivalents that are readily convertible to cash are stated at cost, which approximates market value. The Company considers all highly liquid investments purchased with an original maturity of three months or less to be cash equivalents. Cash equivalents consist primarily of amounts invested in money market funds.

Restricted Cash

Restricted cash at December 31, 2014 and 2015, consisted of cash balances primarily held as security in connection with the Company's corporate credit card.

Available-for-Sale Securities

All marketable securities, have been classified as "available-for-sale" and are carried at estimated fair value as determined based upon quoted market prices or pricing models for similar securities. Management determines the appropriate classification of its marketable securities at the time of purchase and reevaluates such designation as of each balance sheet date. Short-term marketable securities have maturities less than 365 days as of the balance sheet date. Long-term marketable securities have maturities greater than 365 days as of the balance sheet date. Unrealized gains and losses are excluded from earnings and are reported as a component of comprehensive loss. Realized gains and losses and declines in fair value judged to be other than temporary, if any, on available-for-sale securities are included in interest income. The cost of securities sold is based on the specific-identification method. Interest on marketable securities is included in interest income.

2. Summary of Significant Accounting Policies (Continued)

Fair Value of Financial Instruments

Fair value accounting is applied for all financial assets and liabilities that are recognized or disclosed at fair value in the consolidated financial statements on a recurring basis (at least annually). The carrying amount of the Company's financial instruments, including cash and cash equivalents, accounts payable and accrued expenses and other payables approximate fair value due to their short term maturities. See Note 3. Fair Value Measurements regarding the fair value of the Company's available-for-sale securities, redeemable convertible preferred stock tranche liability and redeemable convertible preferred stock warrant liability.

Property and Equipment

Property and equipment are stated at cost, net of accumulated depreciation. Depreciation is computed using the straight-line method over the estimated useful lives of the assets, ranging from three to five years. Leasehold improvements are amortized over the shorter of the lease term or the estimated useful lives of the assets. Maintenance and repairs are charged to expense as incurred. When assets are retired or otherwise disposed of, the cost and accumulated depreciation are removed from the consolidated balance sheet and any resulting gain or loss is reflected in operations in the period realized.

Impairment of Long-Lived Assets

The Company reviews long-lived assets, primarily comprised of property and equipment, for impairment or whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. Recoverability is measured by comparison of the carrying amount to the future net cash flows which the assets are expected to generate. If such assets are considered to be impaired, the impairment to be recognized is measured as the amount by which the carrying amount of the assets exceeds the projected discounted future net cash flows arising from the asset. There have been no such impairments of long-lived assets for any of the periods presented.

Accrued Research and Development Costs

The Company accrues for estimated costs of research and development activities conducted by third-party service providers, which include the conduct of pre-clinical studies and clinical trials, and contract manufacturing activities. The Company records the estimated costs of research and development activities based upon the estimated amount of services provided but not yet invoiced, and include these costs in accrued liabilities in the consolidated balance sheets and within research and development expense in the consolidated statements of operations. These costs are a significant component of the Company's research and development expenses. The Company accrues for these costs based on factors such as estimates of the work completed and in accordance with agreements established with its third-party service providers. The Company makes significant judgments and estimates in determining the accrued liabilities balance in each reporting period. As actual costs become known, the Company adjusts its accrued liabilities. The Company has not experienced any material differences between accrued costs and actual costs incurred. However, the status and timing of actual services performed, number of patients enrolled, and the rate of patient enrollments may vary from the Company's estimates, resulting in adjustments to expense in future periods. Changes in these estimates that result in material changes to the Company's accruals could materially affect the Company's results of operations.

2. Summary of Significant Accounting Policies (Continued)

Comprehensive Loss

Comprehensive loss represents all changes in stockholders' deficit except those resulting from and distributions to stockholders. The Company's foreign currency translation and unrealized gains and losses on available-for-sale securities represent the only components of other comprehensive loss that are excluded from the reported net loss and that are presented in the consolidated statements of comprehensive loss.

Income Taxes

The Company uses the asset and liability method to account for income taxes in accordance with the authoritative guidance for income taxes. Under this method, deferred tax assets and liabilities are determined based on future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases, and tax loss and credit carryforwards. Deferred tax assets and liabilities are measured using enacted tax rates applied to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in income in the period that includes the enactment date. A valuation allowance is established when necessary to reduce deferred tax assets to the amount expected to be realized.

The Company recognizes the effect of income tax positions only if those positions are more likely than not of being sustained. Recognized income tax positions are measured at the largest amount that is greater than 50% likely of being realized. Changes in recognition or measurement are reflected in the period in which the change in judgment occurs. The Company records interest and penalties related to unrecognized tax benefits in income tax expense. To date, there have been no interest or penalties recorded in relation to the unrecognized tax benefits.

Research and Development Costs

Research and development costs are expensed as incurred and consist of salaries and benefits, stock-based compensation expense, lab supplies and facility costs, as well as fees paid to others that conduct certain research and development activities on the Company's behalf.

Research and Development Incentive Grant

The Company is eligible under the AusIndustry research and tax development tax incentive program to obtain a cash amount from the Australian Taxation Office (ATO). The tax incentive is available to the Company on the basis of specific criteria with which the Company must comply. Specifically, the Company must have revenue of less than AUD 20.0 million and cannot be controlled by income tax exempt entities. These research and development tax incentives are recognized as contra research and development expense when the right to receive has been attained and funds are considered to be collectible. The tax incentive is denominated in Australian dollars and, therefore, the related receivable is remeasured into U.S. dollars as of each reporting date.

SBIR Grant

In September 2015, the Company was awarded a Phase 1 Small Business Innovation Research (SBIR) Grant from the National Institute of Diabetes and Digestive and Kidney Diseases of the National Institutes of Health (NIH) in support of research on orally stable antagonist peptides of the interleukin-23 (IL-23) receptor as

2. Summary of Significant Accounting Policies (Continued)

potential treatments for inflammatory bowel diseases. The Company recorded the eligible costs incurred under the SBIR grant as a reduction of research and development expenses and as receivable as of December 31, 2015.

Redeemable Convertible Preferred Stock Tranche Liability

The Company has determined that the Company's obligation to issue additional shares of the Company's redeemable convertible preferred stock represents a freestanding financial instrument, which was accounted for as a liability. The freestanding redeemable convertible preferred stock tranche liability was initially recorded at fair value, with fair value changes recognized in the consolidated statements of operations and comprehensive loss. At the time of the exercise or expiration of the Company's obligation, any remaining value of the redeemable convertible preferred stock tranche liability is reclassified to redeemable convertible preferred stock with no further remeasurement required.

Redeemable Convertible Preferred Stock Warrant Liability

The Company has accounted for its freestanding warrants to purchase shares of the Company's redeemable convertible preferred stock as liabilities at fair value upon issuance. At the end of each reporting period, changes in estimated fair value during the period are recorded in the consolidated statements of operations. The Company will continue to adjust the warrant liability for changes in fair value until the earlier of the expiration on May 10, 2016 or exercise of the warrants, and no further remeasurement is required.

Stock-based Compensation

The Company measures its stock-based awards made to employees based on the estimated fair values of the awards as of the grant date using the Black-Scholes option-pricing model. Stock-based compensation expense is recognized over the requisite service period using the straight-line method and is based on the value of the portion of stock-based payment awards that is ultimately expected to vest. As such, the Company's stock-based compensation is reduced for the estimated forfeitures at the date of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates.

Stock-based compensation expense for options granted to non-employees as consideration for services received is measured on the date of performance at the fair value of the consideration received or the fair value of the equity instruments issued, using the Black-Scholes option-pricing model, whichever can be more reliably measured. Compensation expense for options granted to non-employees is periodically remeasured as the underlying options vest.

Net Loss per Share Attributable to Common Stockholders

Basic net loss per share attributable to common stockholders is calculated by dividing the net loss attributable to common stockholders by the weighted average number of shares of common stock outstanding during the period, without consideration of potentially dilutive securities. The net loss attributable to common stockholders is calculated by adjusting the net loss of the Company for the accretion on the redeemable convertible preferred stock. Diluted net loss per share attributable to common stockholders is the same as basic net loss per share attributable to common stockholders for all periods presented since the effect of potentially dilutive securities are anti-dilutive given the net loss of the Company.

2. Summary of Significant Accounting Policies (Continued)

Unaudited Pro Forma Net Loss per Share Attributable to Common Stockholders

The unaudited pro forma basic and diluted net loss per share attributable to common stockholders has been computed to give effect to the conversion of the shares of redeemable convertible preferred stock into common stock as if such conversion had occurred at the earlier of the beginning of the period or the date of issuance, if later. Also, the numerator in the pro forma basic and diluted net loss per share attributable to common stockholders calculation has been adjusted to remove gains or losses resulting from the remeasurement of the redeemable convertible preferred stock warrant liability as the warrants will be reclassified to additional paid-in capital. The unaudited pro forma net loss per share attributable to common stockholders does not include the shares to be sold and related proceeds to be received from the proposed initial public offering.

Recent Accounting Pronouncements

In August 2014, the FASB issued ASU No. 2014-15, *Disclosure of Uncertainties About an Entity's Ability to Continue as a Going Concern*. ASU 2014-15 requires management to perform interim and annual assessments of an entity's ability to continue as a going concern within one year of the date the financial statements are issued and provides guidance on determining when and how to disclose going concern uncertainties in the financial statements. Certain disclosures will be required if conditions give rise to substantial doubt about an entity's ability to continue as a going concern. ASU 2014-15 applies to all entities and is effective for annual and interim reporting periods ending after December 15, 2016, with early adoption permitted. The Company is currently evaluating the effect the adoption of this guidance will have, if any, on its consolidated financial statements.

In November 2015, FASB issued ASU No. 2015-17, *Income Taxes (Topic 740): Balance Sheet Classification of Deferred Taxes*, which is intended to simplify and improve how deferred taxes are classified on the balance sheet. The guidance in this ASU eliminates the current requirement to present deferred tax assets and liabilities as current and noncurrent in a classified balance sheet and now requires entities to classify all deferred tax assets and liabilities as noncurrent. The guidance is effective for annual periods beginning after December 15, 2016 and for interim periods within those annual periods though early adoption is permitted. The Company does not expect that the adoption of the guidance will have a material effect on the Company's consolidated financial statements.

In February 2016, the FASB issued ASU No. 2016-02, *Leases* (Topic 842). Under the new guidance, (with the exception of short-term leases) at the commencement date, lessees will be required to recognize a lease liability and a right-of-use asset. Lessor accounting is largely unchanged, while lessees will no longer be provided with a source of off-balance sheet financing. Public business entities should apply the amendments in ASU 2016-02 for fiscal years beginning after December 15, 2018, including interim periods within those fiscal years (January 1, 2019, for us). Early application is permitted. Lessees (for capital and operating leases) must apply a modified retrospective transition approach for leases existing at, or entered into after, the beginning of the earliest comparative period presented in the financial statements. The modified retrospective approach would not require any transition accounting for leases that expired before the earliest comparative period presented. The Company is currently evaluating the impact that the guidance will have on its consolidated financial statements.

In March 2016, the FASB issued ASU 2016-09 Compensation-Stock Compensation (Topic 718) Improvements to Employee Share-Based Payment Accounting, which is intended to simplify several aspects of the accounting for employee share-based payment transactions, including the income tax consequences, the determination of forfeiture rates, classification of awards as either equity or liabilities, and classification on the statement of cash flows. This ASU is effective for fiscal years and interim periods within those years beginning

2. Summary of Significant Accounting Policies (Continued)

after December 15, 2016, and early adoption is permitted. The Company is currently evaluating the impact that the adoption of ASU 2016-09 will have on its consolidated financial statements and related disclosures.

3. Fair Value Measurements

Financial assets and liabilities are recorded at fair value. The accounting guidance for fair value provides a framework for measuring fair value, clarifies the definition of fair value and expands disclosures regarding fair value measurements. Fair value is defined as the price that would be received to sell an asset or paid to transfer a liability (an exit price) in an orderly transaction between market participants at the reporting date. The accounting guidance establishes a three-tiered hierarchy, which prioritizes the inputs used in the valuation methodologies in measuring fair value as follows:

Level 1—Inputs are unadjusted quoted prices in active markets for identical assets or liabilities at the measurement date.

Level 2—Inputs (other than quoted market prices included in Level 1) are either directly or indirectly observable for the asset or liability through correlation with market data at the measurement date and for the duration of the instrument's anticipated life.

Level 3—Inputs reflect management's best estimate of what market participants would use in pricing the asset or liability at the measurement date. Consideration is given to the risk inherent in the valuation technique and the risk inherent in the inputs to the model.

In determining fair value, the Company utilizes quoted market prices, broker or dealer quotation, or valuation techniques that maximize the use of observable inputs and minimize the use of unobservable inputs to the extent possible as well as considers counterparty credit risk in its assessment of fair value.

3. Fair Value Measurements (Continued)

The following table presents the fair value of the Company's financial assets and liabilities determined using the inputs defined above (amounts in thousands).

	December 31, 2014			
	Level 1	Level 2	Level 3	Total
Liabilities:				
Redeemable convertible preferred stock warrant liability	$ —	$ —	$1,023	$ 1,023
Total financial liabilities	$ —	$ —	$1,023	$ 1,023

	December 31, 2015			
	Level 1	Level 2	Level 3	Total
Assets:				
Money market funds(a)	$2,136	$ —	$ —	$ 2,136
Corporate bonds(b)	—	7,368	—	7,368
Commercial paper(b)	—	500	—	500
Total financial assets	$2,136	$7,868	$ —	$10,004
Liabilities:				
Redeemable convertible preferred stock tranche liability	$ —	$ —	$1,643	$ 1,643
Redeemable convertible preferred stock warrant liability	—	—	480	480
Total financial liabilities	$ —	$ —	$2,123	$ 2,123

(a) Included in cash and cash equivalents
(b) Included in available-for-sale securities

The corporate bonds and commercial paper are classified as Level 2 as they were valued based upon quoted market prices for similar instruments in active markets, quoted prices for identical or similar instruments in markets that are not active and model-based valuation techniques for which all significant inputs are observable in the market or can be corroborated by observable market data for substantially the full term of the assets.

The fair value measurements of the redeemable convertible preferred stock tranche liability and the redeemable convertible preferred stock warrant liability are based on significant inputs not observed in the market and thus represent a Level 3 measurement. Level 3 instruments are valued based on unobservable inputs that are supported by little or no market activity and reflect the Company's assumptions in measuring fair value.

The redeemable convertible preferred stock tranche liability stems from the initial sale of the Company's Series B and Series C redeemable convertible preferred stock wherein the Company was obligated to sell additional shares in subsequent closings contingent upon a majority of the stockholders of the outstanding redeemable convertible preferred stock and/or the achievement of certain development milestones. The subsequent closings were deemed to be freestanding financial instruments that were at the option of the holders. The Company estimates the fair value of this liability using a one-step binomial lattice model in combination with Option Pricing Model. The change in fair value is recognized as a gain or loss in the consolidated statements of operations. See Note 9 for further discussion on the redeemable convertible preferred stock liability and related valuations.

3. Fair Value Measurements (Continued)

The determination of the fair value of the redeemable convertible preferred stock warrant liability is discussed in Note 7. Generally, increases or decreases in the fair value of the underlying redeemable convertible preferred stock would result in a directionally similar impact in the fair value measurement of the warrant liability.

The following table sets forth a summary of the changes in the fair value of the Company's Level 3 financial instruments as follows (in thousands):

	Year Ended December 31,	
	2014	2015
Redeemable Convertible Preferred Stock Tranche Liability:		
Beginning balance	$ 1,411	$ —
Issuance of Series C redeemable convertible preferred stock tranche liability	—	1,017
Change in fair value upon revaluation	897	626
Settlement of redeemable convertible preferred stock tranche liability due to issue of Series B redeemable convertible preferred shares	(2,308)	—
Ending balance	$ —	$1,643

	Year Ended December 31,	
	2014	2015
Redeemable Convertible Preferred Stock Warrant Liability:		
Beginning balance	$ 151	$1,023
Change in fair value upon revaluation	872	(543)
Ending balance	$1,023	$ 480

4. Balance Sheet Components

Cash Equivalents and Available-for-sale Securities

Cash equivalents and available-for-sale securities consisted of the following (in thousands):

	December 31, 2015			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Money market funds	$ 2,136	$ —	$ —	$ 2,136
Corporate bonds	7,373	—	(5)	7,368
Commercial paper	500	—	—	500
Total cash equivalents and available-for-sale securities	$10,009	$ —	$ (5)	$10,004
Classified as:				
Cash equivalents				$ 2,136
Available-for-sale securities				7,868
Total cash equivalents and available-for-sale securities				$10,004

4. Balance Sheet Components (Continued)

All available-for-sale securities held as of December 31, 2015 had contractual maturities of less than one year. There have been no significant realized gains or losses on available-for-sale securities for the periods presented.

Prepaid Expenses and Other Current Assets

Prepaid expenses and other current assets consisted of the following (in thousands):

	December 31,	
	2014	2015
Prepaid manufacturing of clinical materials	$—	$1,253
Other	56	305
Prepaid expenses and other current assets	$56	$1,558

Property and Equipment, Net

Property and equipment, net consisted of the following (in thousands):

	December 31,	
	2014	2015
Laboratory equipment	$1,089	$ 1,452
Furniture and computer equipment	107	140
Leasehold improvements	46	48
Total property and equipment	1,242	1,640
Less: accumulated depreciation and amortization	(827)	(1,031)
Property and equipment, net	$ 415	$ 609

Depreciation expense for the years ended December 31, 2014 and 2015 was $258,000 and $247,000, respectively. As of December 31, 2014 and 2015, $39,000 and $51,000, respectively, property and equipment, net, were located in Australia. The remainder of the assets are located in the United States.

Accrued Expenses and Other Payables

Accrued expenses and other payables consisted of the following (in thousands):

	December 31,	
	2014	2015
Accrued employee related expenses	$ 559	$ 754
Accrued contract research	345	976
Accrued expenses and other payables	97	149
Accrued expenses and other payables	$1,001	$1,879

5. Government Grants

Research and Development Tax Incentive

The Company recognized AUD 639,000 ($577,000) and AUD 978,000 ($736,000) as a reduction of research and development expenses for the years ended December 31, 2014 and 2015, respectively, in connection with the Research and Development Tax Incentive from Australia. As of December 31, 2014 and 2015, the research and development tax credit receivable was AUD 639,000 ($523,000) and AUD 978,000 ($715,000), respectively.

SBIR Grant

In September 2015, the Company was awarded a Phase 1 SBIR Grant from the National Institute of Diabetes and Digestive and Kidney Diseases of the NIH in support of research on orally stable antagonist peptide of the interleukin-23 receptor (IL-23R) as potential treatments for inflammatory bowel diseases (IBD). The Company recognizes contra research and development when expenses related to the grant have been incurred and the grant funds become contractually due from NIH. The total grant award was $224,000 and is for the period from September 2015 to August 2016. The Company recorded $155,000 as a reduction of research and development expenses for the year ended December 31, 2015. The Company recorded a receivable for $155,000 as of December 31, 2015 to reflect that the eligible costs incurred under the grant.

6. Commitments and Contingencies

Lease Arrangements

The Company leases its facility under a noncancelable operating lease that expires in April 2018. In August 2015, the Company further amended the lease to expand its square footage of occupancy. The term for the expanded space will also terminate in April 2018. The Company has provided a security deposit of $30,000 as collateral for the lease, which is included in other assets on the consolidated balance sheets.

The following table summarizes the Company's future minimum lease payments as of December 31, 2015 (in thousands):

	Amount
Year Ending December 31:	
2016	$372
2017	328
2018	74
Total	$774

The Company's rent expense was $184,000 and $280,000 for the years ended December 31, 2014 and 2015, respectively. Rent expense is recognized on a straight-line basis over the term of the leases and accordingly, the Company records the difference between cash rent payments and the recognition of rent expense as a deferred rent liability.

Indemnifications

In the ordinary course of business, the Company enters into agreements that may include indemnification provisions. Pursuant to such agreements, the Company may indemnify, hold harmless and defend an indemnified party for losses suffered or incurred by the indemnified party. Some of the provisions will limit losses to those

6. Commitments and Contingencies (Continued)

arising from third party actions. In some cases, the indemnification will continue after the termination of the agreement. The maximum potential amount of future payments the Company could be required to make under these provisions is not determinable. The Company has also entered into indemnification agreements with its directors and officers that may require the Company to indemnify its directors and officers against liabilities that may arise by reason of their status or service as directors or officers to the fullest extent permitted by California corporate law. The Company currently has directors' and officers' insurance. To date, the Company has not incurred material costs to defend lawsuits or settle claims related to the indemnification agreements. The Company believes that the fair value of these indemnification agreements is minimal and has not accrued any amounts for the obligations.

7. Preferred Stock Warrants

In connection with the Series B redeemable convertible preferred stock financing, the Company issued warrants to purchase 4,000,000 shares of Series B redeemable convertible preferred stock at an exercise price of $0.01 per share. These warrants will become exercisable only when certain milestones are met on programs begun as a result of collaborations entered into in 2011 and 2012. In particular, 50% of the warrants are exercisable upon the Company publicly announcing its first Investigational New Drug (IND) candidate to the extent such IND candidate is a result of, or related to, the Company's previous collaboration(s) with Ironwood Pharmaceuticals and/or Zealand Pharma A/S, and the balance are exercisable upon the first dosing of a human patient in a clinical trial that is a result of, or related to, the Company's previous collaboration(s) with Ironwood Pharmaceuticals and/or Zealand Pharma A/S. In August 2013, the initial closing date for the Series B financing, the Company issued 2,000,000 of the warrants (First Tranche Warrants). On August 15, 2014, in connection with the closing of the Series B second tranche financing, the Company issued the remaining 2,000,000 warrants (Second Tranche Warrants).

The fair value of the warrants at the issuance date was an aggregate of $783,000, determined using a one-step binomial lattice model in combination with Option Pricing Model based on the following assumptions: an expected term of 2.0 years, risk-free interest rate of 0.26%, volatility of 45.0% and probability of exercisability of 94% and 75% for first tranche and second tranche, respectively. The warrants were accounted for as a warrant liability. The fair value of the warrants in August 2014 was an aggregate of $618,000, determined using a one-step binomial lattice model in combination with the Option Pricing Model based on the following assumptions: an expected term of 2.0 years, risk-free interest rate of 0.47%, volatility of 41.0% and probability of exercisability of 50% and 0% for first tranche and second tranche, respectively. The fair value of the warrants outstanding as of December 31, 2014 was remeasured at $1.0 million, determined using a one-step binomial lattice model in combination with the Option Pricing Model based on the following assumptions: risk-free interest rate of 0.67%, expected life of 2.0 years and expected volatility of 46.0% and probability of exercisability of 75% and 0% for first tranche and second tranche, respectively. The fair value of the warrants outstanding as of December 31, 2015 was remeasured at $480,000, determined using the binomial option pricing model and the following assumptions: risk-free interest rate of 0.90%, expected life of 1.6 years and expected volatility of 57.0% and probability of exercisability of 95% and 0% for first tranche and second tranche, respectively.

As of December 31, 2015, the milestones for both the First Tranche and Second Tranche Warrants were not met. These warrants will expire on May 10, 2016. The change in fair value of the redeemable convertible preferred stock warrant as of December 31, 2014 and 2015 was recorded in the consolidated statements of operations.

In March 2016, the Company made a public announcement related to a pre-clinical candidate which triggered the achievement of the milestone and warrants to purchase 2,000,000 shares of Series B redeemable convertible preferred stock became exercisable as of that date.

8. Redeemable Convertible Preferred Stock

The table below provides information on the Company's redeemable convertible preferred stock as of December 31, 2014 (in thousands, except shares and original issue price):

	Original Issue Price	Shares		Carrying Value	Aggregate Liquidation Preference
		Authorized	Issued and Outstanding		
Series A	$1.00	9,231,041	6,037,500	$ 1,751	$ 6,038
Series B	$0.50	42,000,000	36,000,000	18,825	18,000
Total redeemable convertible preferred stock		51,231,041	42,037,500	$20,576	$24,038

The table below provides information on the Company's redeemable convertible preferred stock as of December 31, 2015 (in thousands, except shares and original issue price):

	Original Issue Price	Shares		Carrying Value	Aggregate Liquidation Preference
		Authorized	Issued and Outstanding		
Series A	$1.00	6,037,500	6,037,500	$ 1,751	$ 6,038
Series B	$0.50	40,000,000	36,000,000	18,825	18,000
Series C	$0.4979	80,337,411	35,147,617	16,420	17,500
Total redeemable convertible preferred stock		126,374,911	77,185,117	$36,996	$41,538

The holders of redeemable convertible preferred stock have various rights and preferences as follows:

Voting

Each holder of shares of redeemable convertible preferred stock is entitled to the number of votes equal to the number of shares of common stock into which such shares of redeemable convertible preferred stock could be converted and has voting rights and powers equal to the voting rights and powers of the common stock, and except as provided by law or by other provisions of the Certificate of Incorporation, shall vote together with the common stock as a single class on an as-converted basis on all matters as to which holders of common stock have the right to vote.

The holders of Series A, B, and C redeemable convertible preferred stock, each voting separately as a single class, are entitled to elect three members of the Company's Board of Directors. All remaining members of the Company's Board of Directors are elected by the holders of the common stock and any other series or class of voting stock, including the Series A, B and C redeemable convertible preferred stock, exclusively and voting together as a single class.

Dividends

The holders of shares of Series A, B and C redeemable convertible preferred stock are entitled to receive dividends, when and if, declared by the Company's Board of Directors. Dividends are noncumulative and none were declared as of December 31, 2015.

8. Redeemable Convertible Preferred Stock (Continued)

Liquidation Preferences

In the event of (A) any sale, transfer of other disposition of the Company (or any subsidiary of the Company) of all or substantially all of the assets of the Company or its subsidiaries (taken as a whole), (B) any transaction or series of transactions (including any reorganization, share exchange, consolidation or merger of the Company with or into any other entity) (x) in which the holders of the Company's outstanding common stock immediately before the first such transaction do not, immediately after any other such transaction, retain stock or other equity interests representing at least fifty percent (50%) of the voting power of the surviving entity of such transaction or (y) in which at least fifty percent (50%) of the Company's outstanding capital stock is transferred or (C) a liquidation, dissolution or winding up of the Company, the holders of Series C redeemable convertible preferred stock are entitled to receive, prior to and in preference to any distribution to the holders of Series A redeemable convertible preferred stock and Series B redeemable convertible preferred stock and common stock, an amount equal to $0.4979 per share, plus any declared but unpaid dividends on such shares. If upon occurrence of such an event, the assets and funds to be distributed among the holders of Series C redeemable convertible preferred stock are insufficient to permit the payment to such holders, the entire assets and funds of the Company legally available for distribution will be distributed ratably among the holders of Series C redeemable convertible preferred stock. After completion of the distribution to the holders of Series C redeemable convertible preferred stock, the holders of Series B redeemable convertible preferred stock are entitled to receive, prior and in preference to holders of Series A redeemable convertible preferred stock and common stock, an amount equal to $0.50 per share, plus any declared and unpaid dividends. If upon occurrence of such an event, the assets and funds to be distributed among the holders of Series B redeemable convertible preferred stock are insufficient to permit the payment to such holders, the assets and funds of the Company legally available for distribution will be distributed ratably among the holders of Series B redeemable convertible preferred stock. After completion of the distribution to the holders of Series B redeemable convertible preferred stock and Series C redeemable convertible preferred stock, the holders of Series A redeemable convertible preferred stock are entitled to receive, prior to and in preference to the holders of common stock, an amount equal to $1.00 per share, plus any declared and unpaid dividends. If upon occurrence of such an event the assets and funds to be distributed among the holders of Series A redeemable convertible preferred stock are insufficient to permit the payment to such holders, the assets and funds of the Company legally available for distribution will be distributed ratably among the holders of Series A redeemable convertible preferred stock. All of the remaining assets, if any, will be distributed to the holders of redeemable convertible preferred stock and common stock pro-rata based on the number of common stock held by each holder on an as converted basis.

Conversion

Each share of Series A, Series B and Series C redeemable convertible preferred stock is convertible, at the option of the holder, into the number of shares of common stock determined by dividing the original issue price of such class of redeemable convertible preferred stock by the conversion price applicable to such class of redeemable convertible preferred stock in effect on the date of conversion. The conversion price per share for Series A, Series B and Series C redeemable convertible preferred stock is $7.25, $7.25 and $7.22 per share, respectively. The conversion price is subject to adjustment from time to time. As of December 31, 2014 and 2015, each share of redeemable convertible preferred stock will convert into common stock on a 1-for-14.5 basis.

Each share of Series A, Series B and Series C redeemable convertible preferred stock is convertible into common stock automatically and immediately upon the earlier of (i) the closing of a Qualified IPO, or (ii) the Company's receipt of a written request for such conversion from (i) the holders of a majority of the then

8. Redeemable Convertible Preferred Stock (Continued)

outstanding shares of redeemable convertible preferred stock and (ii) the holders of a majority of the then outstanding shares of Series C redeemable convertible preferred stock.

Redemption

The Series A redeemable convertible preferred stock is redeemable at the election of at least 60% of the holders of Series A redeemable convertible preferred stock, on or after the redemption in full of all outstanding shares of Series B and Series C redeemable convertible preferred stock, for a price equal to the original issue price, plus all declared but unpaid dividends, in a single installment commencing no later than 90 days after receipt by the Company of the redemption notice.

The Series B redeemable convertible preferred stock is redeemable at the election of the majority of the holders of Series B redeemable convertible preferred stock, on or after the redemption in full of all outstanding shares of Series C redeemable convertible preferred stock, for a price equal to the greater (i) of the original issue price, plus all declared but unpaid dividends or (ii) and the fair market value per share of the Series B redeemable convertible preferred stock on the date of such redemption election. The Company shall effect such redemption by paying Series B holders in a single installment commencing no later than 90 days after receipt by the Company of the redemption notice.

The Series C redeemable convertible preferred stock is redeemable at the election of the majority of the holders of Series C redeemable convertible preferred stock, on or after the seventh anniversary of the Series C redeemable convertible preferred stock issue date (or July 2022), for a price equal to the greater of (i) the original issue price, plus all declared but unpaid dividends, or (ii) and the fair market value per share of the Series C redeemable convertible preferred stock on the date of such redemption election. The Company shall effect such redemption by paying Series C holders in a single installment commencing no later than 90 days after receipt by the Company of the redemption notice.

As only the passage of time is required for Series A, B and C to become redeemable, the Company is accreting on an effective interest method the carrying value of Series A, B and C to their redemption value over the period from the respective date of issuance to July 2022, (the earliest redemption date). In the event of a change of control of the Company, proceeds will be distributed in accordance with the liquidation preferences set forth in the Company's Amended and Restated Certificate of Incorporation unless the holders of redeemable convertible preferred stock have converted their redeemable convertible preferred stock into shares of common stock. Therefore, redeemable convertible preferred stock is classified outside of stockholders' deficit on the consolidated balance sheets, as Series A, B and C redeemable convertible preferred stock can be redeemed and as events triggering the liquidation preferences are not solely within the Company's control.

The Company recorded $146,000 and $75,000 for the accretion of the redeemable convertible preferred stock during the years ended December 31, 2014 and 2015. The accretion was recorded as an offset to the additional paid in capital until such balance was depleted and any remaining accretion was recorded to accumulated deficit.

9. Redeemable Convertible Preferred Stock Tranche Liability

Series B Financing

In May 2013, the Company entered into the Series B Preferred Stock Purchase Agreement (the Series B Agreement) for the issuance of up to 38,000,000 shares of Series B redeemable convertible preferred stock at a

9. Redeemable Convertible Preferred Stock Tranche Liability (Continued)

price of $0.50 per share, in multiple closing. The initial closing occurred in 2013, whereby 18,000,000 shares of Series B redeemable convertible preferred stock were issued for gross cash proceeds of $9.0 million. According to the initial terms of the Series B Agreement, the Company could issue 18,000,000 shares under the same terms as the initial closing, in a subsequent closing (Series B Second Tranche) contingent upon the achievement of certain development milestones. As discussed in Note 7 above, the Company issued a warrant to purchase 4,000,000 shares of Series B redeemable convertible preferred stock at an exercise price of $0.01 per share in connection with the Series B redeemable convertible preferred stock financing.

The Company recorded the redeemable convertible preferred stock liability incurred in connection with its Series B redeemable convertible preferred stock financing as a derivative financial instrument liability at the fair value on the date of issuance, and remeasured it on each subsequent balance sheet date. The Series B redeemable convertible preferred stock liability stems from the initial sale of Series B redeemable convertible preferred stock wherein the Company was obligated to sell additional shares in subsequent closings contingent upon the achievement of certain development milestones and approval from the Company's Board of Directors. The subsequent closings were deemed to be freestanding financial instruments that were outside the control of the Company. The changes in fair value are recognized as a gain or loss in the statements of operations and liability is remeasured at each reporting period and settlement of the related Series B Second Tranche. The Company estimated the fair value of this liability using the binomial lattice based option pricing model that included assumptions of probability of achievement of the development milestones or funding of the financing, stock price, expected term and risk-free interest rate.

On the date of the initial closing, the Company recorded a Series B redeemable convertible preferred stock liability of $866,000 as fair value of the obligation/right for the Series B Second Tranche. The fair value of the redeemable convertible preferred stock liability on the date of the initial closing was determined using a one-step binomial lattice model in combination with option pricing method based on the following assumptions: 80% probability of achievement of the development milestones, stock price of $0.50 per share, expected term of 1.64 years, and risk-free rate of 0.3%.

In August 2014, the Company completed the closing of the Series B Second Tranche and issued 18,000,000 shares of Series B redeemable convertible preferred stock for gross cash proceeds of $9.0 million. At this time the Series B redeemable convertible preferred stock liability was remeasured at $2.3 million using a one-step binomial lattice model in combination with option pricing method based on the following assumptions: 100% probability of achievement of the development milestones, stock price of $0.50 per share, expected term of 0 years and risk-free rate of 0.5%. Upon the closing of the Series B Second Tranche, the Series B redeemable convertible preferred stock liability was terminated and the balance of the liability of $2.3 million was reclassified to redeemable convertible preferred stock.

For the year ended December 31, 2014, the Company recorded a total charge of $897,000 for the changes in the fair value of the Series B redeemable convertible preferred stock liability in the consolidated statement of operations.

Series C Financing

In July 2015, the Company entered into the Series C Preferred Stock Purchase Agreement (the Series C Agreement) for the issuance of up to 80,337,411 shares of Series C redeemable convertible preferred stock at a price of $0.4979 per share, in multiple closings. The initial closing occurred on July 10, 2015, whereby 35,147,617 shares of Series C redeemable convertible preferred stock were issued for gross proceeds of approximately $17.5 million. According to the initial terms of the Series C Agreement, the Company could issue

9. Redeemable Convertible Preferred Stock Tranche Liability (Continued)

45,189,794 additional shares under the same terms as the initial closing, in a subsequent closing (Series C Second Tranche) contingent upon the achievement of certain development milestones.

On the date of the initial closing, the Company recorded a Series C redeemable convertible preferred stock liability of $1.0 million, as the fair value of the obligation/right to complete the Series C Second Tranche. The fair value of the Series C redeemable convertible preferred stock liability on the date of the initial closing was determined using a one-step binomial lattice model in combination with the option pricing model based on the following assumptions: 90% probability of achievement of the development milestones, stock price of $0.4979 per share, expected term of 1.0 year, and risk-free rate of 0.5%.

At December 31, 2015, the fair value of the Series C redeemable convertible preferred stock liability was remeasured and determined to be $1.6 million using a one-step binomial lattice model in combination with the option pricing model based on the following assumptions: 95% probability of achievement of the development milestones, stock price of $0.4979 per share, expected term of 0.53 year, and risk-free rate of 0.9%.

For the year ended December 31, 2015, the Company recorded a charge of $626,000 for the change in the fair value of the Series C redeemable convertible preferred stock liability in the consolidated statements of operations.

10. Common Stock

At December 31, 2015, the Company has reserved sufficient shares of common stock for issuance upon conversion of all redeemable convertible preferred stock and exercise of stock options and warrants. Each share of common stock is entitled to one vote. The holders of common stock are also entitled to receive dividends whenever funds are legally available and when declared by the Company's Board of Directors, subject to prior rights of the holders of redeemable convertible preferred stock.

The Company had reserved shares of common stock for issuance, on an as-converted basis, as follows:

	December 31,	
	2014	2015
Redeemable convertible preferred stock outstanding	2,899,134	5,323,103
Options issued and outstanding	476,006	833,178
Options available for future grants	116,832	147,219
Redeemable convertible preferred stock warrants	275,861	275,861
Total	3,767,833	6,579,361

11. Stock Option Plan

In May 2007, the Company established its 2007 Stock Option and Incentive Plan (2007 Plan) which provides for the granting of stock options to employees and consultants of the Company. Options granted under the 2007 Plan may be either incentive stock options (ISOs) or nonqualified stock options (NSOs). ISOs may be granted only to Company employees (including officers and directors who are also employees). NSOs may be granted to Company employees and consultants. As of December 31, 2015, the Company has reserved 1,028,388 shares of common stock for issuance under the 2007 Plan.

11. Stock Option Plan (Continued)

To date, options have a term of ten years and generally vest over a four-year period with one-year cliff vesting.

Activity under the Company's stock option plan is set forth below:

			Options Outstanding		
	Options Available for Grant	Options Outstanding	Weighted-Average Exercise Price Per Share	Weighted-Average Remaining Contractual Life (years)	Aggregate Intrinsic Value
					(in thousands)
Balances at December 31, 2013	70,082	284,879	$1.10	7.92	
Additional options authorized	240,425	—			
Options granted	(199,519)	199,519	1.83		
Options exercised	—	(2,548)	1.30		
Options forfeited	5,844	(5,844)	1.13		
Balances at December 31, 2014	116,832	476,006	1.40	8.04	
Additional options authorized	431,411	—			
Options granted	(408,623)	408,623	1.24		
Options exercised	—	(43,852)	1.30		
Options forfeited	7,599	(7,599)	1.40		
Balances at December 31, 2015	147,219	833,178	$1.33	8.56	$48
Options exercisable—December 31, 2015		233,940	$1.30	7.10	$27
Options vested and expected to vest—December 31, 2015		820,494	$1.33	8.55	$48

The aggregate intrinsic values of options outstanding, exercisable, vested and expected to vest were calculated as the difference between the exercise price of the options and the fair value of the Company's common stock, as determined by the Company's Board of Directors, as of December 31, 2015. The aggregate intrinsic value of options exercised was immaterial for the years ended December 31, 2014 and 2015, respectively.

During the years ended December 31, 2014 and 2015, the estimated weighted-average grant-date fair value of common stock underlying options granted was $0.82 and $0.69 per share, respectively.

11. Stock Option Plan (Continued)

Employee Stock Options Valuation

The fair value of employee and director stock option awards was estimated at the date of grant using a Black-Scholes option-pricing model with the following assumptions:

	Year Ended December 31,	
	2014	2015
Expected term (in years)	6.08	5.89
Expected volatility	64.7%	59.8%
Risk-free interest rate	1.89%	1.57 – 1.58%
Dividend yield	—	—

The fair value of the Company's shares of common stock underlying its stock options has historically been determined by the Company's Board of Directors. Because there has been no public market for the Company's common stock, the Company's Board of Directors has determined fair value of the common stock at the time of grant of the option by considering a number of objective and subjective factors including important developments in the Company's operations, valuations performed by an independent third party, sales of redeemable convertible preferred stock, actual operating results and financial performance, the conditions in the biotechnology industry and the economy in general, the stock price performance and volatility of comparable public companies, and the lack of liquidity of the Company's common stock, among other factors.

In determining the fair value of the options granted, the Company uses the Black-Scholes option-pricing model and assumptions discussed below. Each of these inputs is subjective and generally requires significant judgment to determine.

Expected Term—The Company's expected term represents the period that the Company's options granted are expected to be outstanding and is determined using the simplified method (based on the mid-point between the vesting date and the end of the contractual term). The Company has very limited historical information to develop reasonable expectations about future exercise patterns and post-vesting employment termination behavior for its stock option grants.

Expected Volatility—Since the Company is privately held and does not have any trading history for its common stock, the expected volatility was estimated based on the average volatility for comparable publicly traded biopharmaceutical companies over a period equal to the expected term of the stock option grants. The comparable companies were chosen based on their similar size, stage in the life cycle or area of specialty.

Risk-Free Interest Rate—The risk-free interest rate is based on the U.S. Treasury zero coupon issues in effect at the time of grant for periods corresponding with the expected term of option.

Expected Dividend—The Company has never paid dividends on its common stock and has no plans to pay dividends on its common stock. Therefore, the Company used an expected dividend yield of zero.

11. Stock Option Plan (Continued)

Stock Options Granted to Non-employees

Stock-based compensation related to stock options granted to non-employees is recognized as the stock options are earned. The fair value of the stock options granted is calculated at each reporting date using the Black-Scholes option-pricing model with the following assumptions:

	Year Ended December 31,	
	2014	2015
Expected term (in years)	9.4	6.8
Expected volatility	64.7%	59.8%
Risk-free interest rate	2.34%	1.95%
Dividend yield	—	—

During the years ended December 31, 2014, and 2015, the Company granted 11,805 and 4,816 shares, respectively, to non-employee consultants and recorded stock-based compensation expense of $5,000 and $15,000, respectively.

Stock-Based Compensation

Total stock-based compensation expense recognized for both employees and non-employees was as follows (in thousands):

	Year Ended December 31,	
	2014	2015
Research and development	$17	$39
General and administrative	25	60
Total stock-based compensation expense	$42	$99

As of December 31, 2015 there was $404,000 of total unrecognized stock-based compensation costs that the Company expects to recognize over a period of approximately 3.2 years.

12. Income Taxes

No provision for income taxes was recorded for the years ended December 31, 2014 and 2015. The Company has incurred net operating losses for all the periods presented. The Company has not reflected any benefit of such net operating loss carryforwards in the consolidated financial statements. The Company has established a full valuation allowance against its deferred tax assets due to the uncertainty surrounding the realization of such assets.

12. Income Taxes (Continued)

The effective tax rate of the provision for income taxes differs from the federal statutory rate as follows:

	Year Ended December 31,	
	2014	2015
Federal statutory income tax rate	34.0%	34.0%
State taxes, net of federal benefit	4.1	(2.7)
Foreign tax rate difference	(6.8)	(11.8)
Warrant revaluation	(5.5)	(0.2)
Change in valuation allowance	(26.5)	(19.9)
Other	0.7	0.6
Provision for income taxes	0.0%	0.0%

The components of the deferred tax assets are as follows (in thousands):

	December 31,	
	2014	2015
Deferred tax assets:		
Net operating loss carryforwards	$ 6,874	$ 9,513
Depreciation and amortization	525	480
Accruals/other	205	293
Research and development credits & foreign credits	3	285
Total deferred tax assets	7,607	10,571
Valuation allowance	(7,607)	(10,571)
Net deferred tax assets	$ —	$ —

Realization of the deferred tax assets is dependent upon future taxable income, if any, the amount and timing of which are uncertain. The Company has established a valuation allowance to offset deferred tax assets as of December 31, 2014 and 2015 due to the uncertainty of realizing future tax benefits from its net operating loss carryforwards and other deferred tax assets. The valuation allowance increased by approximately $2.9 million and $3.0 million during the year ended December 31, 2014 and 2015, respectively. The increase in the valuation allowance is mainly related to the increase in net operating loss carryforwards incurred during the respective taxable years.

At December 31, 2015, the Company had net operating loss carryforwards for federal income tax purposes of approximately $20.0 million which are available to offset future taxable income, if any, through 2033 and net operating loss carryforwards for state income tax purposes of approximately $9.4 million which are available to offset future taxable income, if any, through 2033.

At December 31, 2015 the Company also had accumulated Australian tax losses of $8.7 million available for carry forward against future earnings which, under relevant tax laws, do not expire but may not be available under certain circumstances.

Federal and state laws impose substantial restrictions on the utilization of net operating loss and tax credit carryforwards in the event of an ownership change for tax purposes, as defined in Section 382 of the Internal Revenue Code. As a result of such ownership changes, the Company's ability to realize the potential future

12. Income Taxes (Continued)

benefit of tax losses and tax credits that existed at the time of the ownership change may be significantly reduced. The Company's deferred tax asset and related valuation allowance would be reduced as a result.

It is the Company's policy to include penalties and interest expense related to income taxes as a component of other expense, as necessary.

A reconciliation of the beginning and ending amount of unrecognized tax benefits is as follows (in thousands):

	Year Ended December 31,	
	2014	2015
Balance at beginning of year	$—	$ —
Additions based on tax positions related to in prior years	—	690
Additions based on tax positions related to current year	—	115
Balance at end of year	$—	$805

The Company does not expect that its uncertain tax positions will materially change in the next twelve months. The reversal of the uncertain tax benefits would not impact the Company's effective tax rate as the Company continues to maintain a full valuation allowance against its deferred tax assets.

The Company files income tax returns in the United States federal jurisdiction, the State of California and Australia. The Company is not currently under examination by income tax authorities in federal, state or other jurisdictions. The Company's tax returns for 2011 through 2015 remain open for examination due to the carryover of unused net operating losses and tax credits.

13. Net Loss per Share Attributable to Common Stockholders

As the Company had net losses for the years ended December 31, 2014 and 2015, all potential common shares were determined to be anti-dilutive. The following table sets forth the computation of the basic and diluted net loss per share attributable to common stockholders during the years ended December 31, 2014 and 2015 (in thousands, except share and per share data):

	Year Ended December 31,	
	2014	2015
Numerator:		
Net loss	$ (11,072)	$ (14,858)
Accretion of redeemable convertible preferred stock	(146)	(75)
Net loss attributable to common stockholders	$ (11,218)	$ (14,933)
Denominator:		
Weighted-average shares used to compute net loss per common share, basic and diluted	227,197	251,717
Net loss per share attributable to common stockholders, basic and diluted	$ (49.38)	$ (59.32)

13. Net Loss per Share Attributable to Common Stockholders (Continued)

The following outstanding shares of potentially dilutive securities have been excluded from diluted net loss per share calculations for the years ended December 31, 2014 and 2015, because their inclusion would be anti-dilutive:

	Year Ended December 31,	
	2014	2015
Redeemable convertible preferred stock on an as-converted basis	2,899,134	5,323,103
Options to purchase common stock	476,006	833,178
Warrants to purchase redeemable convertible preferred stock on an as-converted basis	275,861	275,861
Total	3,651,001	6,432,142

14. Pro Forma Net Loss per Share Attributable to Common Stockholders (Unaudited)

The following table sets forth (in thousands, except share and per share amounts) the computation of the Company's unaudited pro forma basic and diluted net loss per share attributable to common stockholders after giving effect to the automatic conversion of redeemable convertible preferred stock using the as-if converted method into common stock as though the conversion had occurred at the beginning of the period presented or date of issuance, if later. The numerator in the pro forma basic and diluted net loss per common share calculation has been adjusted to remove gains or losses resulting from the remeasurement of the redeemable convertible preferred stock warrant liability as the warrants will become warrants to purchase common stock and will be reclassified to additional paid-in capital upon the completion of the offering.

	Year Ended December 31, 2015
Net loss	$ (14,858)
Change in fair value of redeemable convertible preferred stock warrant liability	(543)
Net loss used in computing pro forma net loss per common share, basic and diluted	$ (15,401)
Weighted average shares used to compute net loss per share attributable to common stock holders, basic and diluted	251,717
Pro forma adjustment to reflect assumed conversion of redeemable convertible preferred stock	4,061,315
Shares used to compute pro forma net loss per share attributable to common stockholders, basic and diluted	4,313,032
Pro forma net loss per share attributable to common stockholders, basic and diluted	$ (3.57)

The Company corrected an error in the 2015 unaudited pro forma net loss per share calculation, which increased the unaudited pro forma net loss by $1.1 million or $0.25 per share. The Company believes the error in the unaudited pro forma net loss per share calculation to not be material.

15. 401(k) Plan

In March 2012, the Company adopted a retirement and savings plan under Section of 401(k) of Internal Revenue Code (the 401(k) Plan) covering all employees. The 401(k) Plan allows employees to make pre- and post-tax contributions up to the maximum allowable amount set by the IRS. The Company does not make matching contributions to the 401(k) plan on behalf of participants.

16. Subsequent Events

In March 2016, the Company completed the closing of the Series C Second Tranche and issued 45,189,794 shares of Series C redeemable convertible preferred stock for cash proceeds of $22.5 million. Upon the date of closing, the fair value of the tranche liability was remeasured and the liability was reclassified to redeemable convertible preferred stock.

In March 2016, the Company decided to undertake pre-clinical development studies on PTG-300, that was part of an initial research program with a former collaboration partner. The Company owes $250,000 to the former collaboration partner for triggering this development milestone. If the Company initiates a Phase 1 clinical trial for PTG-300, it will owe the former collaboration partner an additional $250,000. If the Company develops and commercializes this compound without a partner it may be required to pay up to an additional aggregate of $128.5 million in future development and commercialization milestones under the agreement. In addition, the Company will pay a low single digit royalty on worldwide net sales of the product.

In March 2016, effective with the closing of the Series C Second Tranche, the number of shares available for issuance under the Company's 2007 Plan was increased by 549,977. Subsequent to December 31, 2015, the Company has granted options for the purchase of an aggregate of 631,273 shares of common stock with a weighted average exercise price of $3.70 per share.

In April 2016, 1,999,998 shares of Series B redeemable convertible preferred stock were issued in connection with the exercise of warrants.

In July 2016, the Company's board of directors approved an amendment to the Company's amended and restated certificate of incorporation to effect a reverse split of the Company's issued and outstanding common stock at a 14.5-for-1 ratio, which was effected on August 1, 2016. The par value and authorized shares of common stock and convertible preferred stock were not adjusted as a result of the reverse split. All issued and outstanding common stock, options to purchase common stock and per share amounts contained in the financial statements have been retroactively adjusted to reflect the reverse stock split for all periods presented. The financial statements have also been retroactively adjusted to reflect a proportional adjustment to the conversion ratio for each series of preferred stock that will be effected in connection with the reverse stock split.

The Company has reviewed and evaluated subsequent events through May 3, 2016, the date the consolidated financial statements were available for issuance. For the reissuance of these consolidated financial statements, the Company has reviewed and evaluated subsequent events through August 1, 2016.

PROTAGONIST THERAPEUTICS, INC.

Condensed Consolidated Balance Sheets

(In thousands, except share data)

	December 31, 2015 (Note 2)	March 31, 2016 (Unaudited)	Pro forma Stockholders' Equity as of March 31, 2016 (Unaudited)
Assets			
Current assets:			
Cash and cash equivalents	$ 4,055	$ 28,629	
Restricted cash	10	10	
Available-for-sale securities	7,868	393	
Research and development tax incentive receivable	715	1,290	
Prepaid expenses and other current assets	1,558	615	
Total current assets	14,206	30,937	
Property and equipment, net	609	753	
Other assets	30	166	
Total assets	$14,845	$ 31,856	
Liabilities, Redeemable Convertible Preferred Stock and Stockholders' (Deficit) Equity			
Current liabilities:			
Accounts payable	$ 1,247	$ 1,890	
Accrued expenses and other payables	1,879	2,580	
Total current liabilities	3,126	4,470	
Redeemable convertible preferred stock tranche liability	1,643	—	
Redeemable convertible preferred stock warrant liability	480	1,005	$ —
Total liabilities	5,249	5,475	
Commitments and contingencies			
Redeemable convertible preferred stock, $0.00001 par value: 126,374,911 shares authorized as of December 31, 2015 and March 31, 2016 (unaudited); 77,185,117 and 122,374,911 shares issued and outstanding as of December 31, 2015 and March 31, 2016 (unaudited), respectively; redemption value of $64,038 as of March 31, 2016	36,996	65,361	—
Stockholders' (deficit) equity:			
Common stock, $0.00001 par value, 160,000,000 shares authorized as of December 31, 2015 and March 31, 2016 (unaudited); 272,409 and 383,910 shares issued and outstanding as of December 31, 2015 and March 31, 2016, respectively; 8,823,551 shares issued and outstanding, pro forma (unaudited)	—	—	—
Additional paid-in capital	118	277	66,643
Accumulated other comprehensive loss	(102)	(95)	(95)
Accumulated deficit	(27,416)	(39,162)	(39,162)
Total stockholders' (deficit) equity	(27,400)	(38,980)	$27,386
Total liabilities, redeemable convertible preferred stock and stockholders' deficit	$14,845	$ 31,856	

The accompanying notes are an integral part of these unaudited condensed consolidated financial statements.

PROTAGONIST THERAPEUTICS, INC.

Condensed Consolidated Statements of Operations

(Unaudited)

(In thousands, except share and per share data)

	Three Months Ended March 31,	
	2015	**2016**
Operating expenses:		
Research and development	$ 2,183	$ 5,625
General and administrative	506	1,415
Total operating expenses	2,689	7,040
Loss from operations	(2,689)	(7,040)
Interest income	1	12
Change in fair value of redeemable convertible preferred stock tranche and warrant liabilities	(9)	(4,719)
Net loss	$ (2,697)	$ (11,747)
Net loss attributable to common stockholders	$ (2,697)	$ (11,787)
Net loss per share attributable to common stockholders, basic and diluted	$ (11.75)	$ (40.96)
Weighted-average shares used to compute net loss per share attributable to common stockholders, basic and diluted	299,483	287,800
Pro forma net loss per share attributable to common stockholders, basic and diluted		$ (1.91)
Pro forma weighted-average shares used to compute net loss per share attributable to common stockholders, basic and diluted		5,884,892

The accompanying notes are an integral part of these unaudited condensed consolidated financial statements.

PROTAGONIST THERAPEUTICS, INC.

Consolidated Statements of Comprehensive Loss

(Unaudited)

(In thousands)

	Three Months Ended March 31,	
	2015	**2016**
Net loss	$(2,697)	$(11,747)
Other comprehensive loss:		
Gain (loss) on translation of foreign operations, net of tax	(16)	2
Unrecognized gain on available-for-sale securities	—	5
Comprehensive loss	$(2,713)	$(11,740)

The accompanying notes are an integral part of these unaudited condensed consolidated financial statements.

PROTAGONIST THERAPEUTICS, INC.

Condensed Consolidated Statements of Cash Flows

(Unaudited)

(In thousands)

	Three Months Ended March 31,	
	2015	2016
CASH FLOWS FROM OPERATING ACTIVITIES		
Net loss	$(2,697)	$(11,747)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	58	73
Amortization of premium on available-for-sale securities	—	82
Stock-based compensation	19	56
Change in fair value associated with redeemable convertible preferred stock tranche liability	—	4,194
Change in fair value of redeemable convertible preferred stock warrant liability	9	525
Changes in operating assets and liabilities:		
Research and development tax credit receivable	(66)	(575)
Prepaid expenses and other current assets	(270)	943
Accounts payable	521	593
Accrued expenses and other payables	(7)	617
Net cash used in operating activities	(2,433)	(5,239)
CASH FLOWS FROM INVESTING ACTIVITIES		
Purchase of property and equipment	(5)	(251)
Proceeds from maturities of investments	—	7,398
Net cash provided by (used in) investing activities	(5)	7,147
CASH FLOWS FROM FINANCING ACTIVITIES		
Proceeds from issuance of redeemable convertible preferred stock, net of issuance costs	—	22,488
Proceeds from issuance of common stock upon exercise of stock options	2	143
Net cash provided by financing activities	2	22,631
Effect on exchange rate changes on cash and cash equivalents	(13)	35
Net increase (decrease) in cash and cash equivalents	(2,449)	24,574
Cash and cash equivalents, beginning of period	9,324	4,055
Cash and cash equivalents, end of period	$ 6,875	$ 28,629
SUPPLEMENTAL DISCLOSURES OF NON-CASH FINANCING INFORMATION:		
Settlement of fair value of redeemable convertible preferred stock liability	$ —	$ 5,837
Accretion of redeemable convertible preferred stock	$ —	$ 40
Deferred offering costs in accounts payable and accrued liabilities	$ —	$ 135

The accompanying notes are an integral part of these unaudited condensed consolidated financial statements.

1. Organization and Description of Business

Protagonist Therapeutics, Inc. (the Company) was incorporated in the state of Delaware on August 22, 2006 and is headquartered in Milpitas, California. The Company is a clinical-stage biopharmaceutical company with a proprietary peptide technology platform focused on discovering and developing new chemical entities to address significant unmet medical needs.

Protagonist Pty Ltd is a wholly-owned subsidiary located in Brisbane, Australia. The Company manages its operations as a single operating segment.

Need for Additional Capital

In the course of its development activities, the Company has sustained operating losses and expects such losses to continue over the next several years. The Company's ultimate success depends on the outcome of its research and development activities. The Company has funded its operations to date primarily through the sale of convertible preferred stock. As of March 31, 2016, the Company had an accumulated deficit of $39.2 million. Management expects to incur additional losses in the future to conduct product research and development and recognizes the need to raise additional capital to fully implement its business plan. The Company intends to raise such capital through the issuance of additional equity. However, if such financing is not available at adequate levels, the Company will need to reevaluate its operating plans.

2. Summary of Significant Accounting Policies

Unaudited Interim Condensed Consolidated Financial Statements

The unaudited interim condensed consolidated financial statements include the accounts of the Company and its wholly owned subsidiary, Protagonist Pty Ltd. All intercompany balances and transactions have been eliminated in consolidation.

The interim condensed consolidated balance sheet as of March 31, 2016, and the condensed consolidated statements of operations, comprehensive loss, and cash flows for the three months ended March 31, 2015 and 2016 are unaudited. The unaudited interim condensed consolidated financial statements have been prepared on the same basis as the annual consolidated financial statements and reflect, in the opinion of management, all adjustments of a normal and recurring nature that are necessary for the fair statement of the Company's financial position as of March 31, 2016 and its results of operations and cash flows for the three months ended March 31, 2015 and 2016. The financial data and the other financial information disclosed in these notes to the condensed consolidated financial statements related to the three-month periods are also unaudited. The results of operations for the three months ended March 31, 2016 are not necessarily indicative of the results to be expected for the year ending December 31, 2016 or for any other future annual or interim period. The balance sheet as of December 31, 2015 included herein was derived from the audited consolidated financial statements as of that date. These consolidated financial statements should be read in conjunction with the Company's audited consolidated financial statements included elsewhere in this prospectus.

Use of Estimates

The preparation of the consolidated financial statements in conformity with U.S. GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities as of the date of the consolidated financial statements and the

2. Summary of Significant Accounting Policies (Continued)

reported amounts of revenues and expenses during the reporting period. On an ongoing basis, management evaluates its estimates, including those related to accruals for research and development activities, fair value of redeemable convertible preferred stock tranche liability, fair value of redeemable convertible preferred stock warrant liability, fair value of common stock, stock-based compensation and income taxes. Management bases these estimates on historical and anticipated results, trends, and various other assumptions that the Company believes are reasonable under the circumstances, including assumptions as to future events. Actual results may differ from those estimates.

Unaudited Pro Forma Consolidated Stockholders' Equity

The unaudited pro forma consolidated stockholders' equity as of March 31, 2016 presents the Company's consolidated stockholders' equity as though all of the Company's outstanding redeemable convertible preferred stock had converted into shares of common stock immediately prior to the completion of a firm commitment underwritten public offering in which the public offering price equals or exceeds 200% of the Series C redeemable convertible preferred stock original issue price (adjusted to reflect subsequent stock dividends, stock splits, or recapitalization) which results in aggregate net proceeds raised that equals or exceeds $40.0 million (a Qualified IPO). In addition, the unaudited pro forma consolidated stockholders' equity assumes the reclassification of the redeemable convertible preferred stock warrant liability to consolidated stockholders' equity as the outstanding warrants to purchase redeemable convertible preferred stock expired on May 10, 2016. The unaudited pro forma consolidated stockholders' equity does not assume any proceeds from the offering.

Cash Equivalents

Cash equivalents that are readily convertible to cash are stated at cost, which approximates market value. The Company considers all highly liquid investments purchased with an original maturity of three months or less to be cash equivalents. Cash equivalents consist primarily of amounts invested in money market funds.

Restricted Cash

Restricted cash consisted of cash balances primarily held as security in connection with the Company's corporate credit card.

Available-for-Sale Securities

All marketable securities, have been classified as "available-for-sale" and are carried at estimated fair value as determined based upon quoted market prices or pricing models for similar securities. Management determines the appropriate classification of its marketable securities at the time of purchase and reevaluates such designation as of each balance sheet date. Short-term marketable securities have maturities less than 365 days as of the balance sheet date. Long-term marketable securities have maturities greater than 365 days as of the balance sheet date. Unrealized gains and losses are excluded from earnings and are reported as a component of comprehensive loss. Realized gains and losses and declines in fair value judged to be other than temporary, if any, on available-for-sale securities are included in interest income. The cost of securities sold is based on the specific-identification method. Interest on marketable securities is included in interest income.

Deferred Offering Costs

Deferred offering costs, which include legal, accounting, printer and filing fees, related to the IPO are capitalized. The deferred offering costs will be offset against proceeds from the IPO upon the effectiveness of the

2. Summary of Significant Accounting Policies (Continued)

offering. In the event that the offering is terminated, all capitalized deferred offering costs will be immediately expensed. As of March 31, 2016, $135,000 of deferred offering costs were capitalized, which are included in other assets on the condensed consolidated balance sheet. There were no such costs capitalized as of December 31, 2015.

Fair Value of Financial Instruments

Fair value accounting is applied for all financial assets and liabilities that are recognized or disclosed at fair value in the consolidated financial statements on a recurring basis (at least annually). The carrying amount of the Company's financial instruments, including cash and cash equivalents, accounts payable and accrued expenses and other payables approximate fair value due to their short term maturities. See Note 3. Fair Value Measurements regarding the fair value of the Company's available-for-sale securities, redeemable convertible preferred stock tranche liability and redeemable convertible preferred stock warrant liability.

Accrued Research and Development Costs

The Company accrues for estimated costs of research and development activities conducted by third-party service providers, which include the conduct of preclinical studies and clinical trials, and contract manufacturing activities. The Company records the estimated costs of research and development activities based upon the estimated amount of services provided but not yet invoiced, and include these costs in accrued liabilities in the consolidated balance sheets and within research and development expense in the consolidated statements of operations. These costs are a significant component of the Company's research and development expenses. The Company accrues for these costs based on factors such as estimates of the work completed and in accordance with agreements established with its third-party service providers. The Company makes significant judgments and estimates in determining the accrued liabilities balance in each reporting period. As actual costs become known, the Company adjusts its accrued liabilities. The Company has not experienced any material differences between accrued costs and actual costs incurred. However, the status and timing of actual services performed, number of patients enrolled, and the rate of patient enrollments may vary from the Company's estimates, resulting in adjustments to expense in future periods. Changes in these estimates that result in material changes to the Company's accruals could materially affect the Company's results of operations.

Research and Development Costs

Research and development costs are expensed as incurred and consist of salaries and benefits, stock-based compensation expense, lab supplies and facility costs, as well as fees paid to others that conduct certain research and development activities on the Company's behalf.

Research and Development Incentive Grant

The Company is eligible under the AusIndustry research and tax development tax incentive program to obtain a cash amount from the Australian Taxation Office (ATO). The tax incentive is available to the Company on the basis of specific criteria with which the Company must comply. Specifically, the Company must have revenue of less than AUD 20.0 million and cannot be controlled by income tax exempt entities. These research and development tax incentives are recognized as contra research and development expense when the right to receive has been attained and funds are considered to be collectible. The tax incentive is denominated in Australian dollars and, therefore, the related receivable is remeasured into U.S. dollars as of each reporting date.

2. Summary of Significant Accounting Policies (Continued)

Under certain conditions, research and development activities conducted outside Australia ("overseas finding") also qualify for the research and development incentive grant. Funds received for overseas finding are at a risk of clawback until substantiation that less than 50% research and development expenditures for a project will be incurred overseas. A deferred tax incentive is recorded upon the cash receipt of the overseas finding funds and a reduction of research and development expense is not recognized until the Company can substantiate that more than 50% of the total project expenditure will occur in Australia.

SBIR Grant

In September 2015, the Company was awarded a Phase 1 Small Business Innovation Research (SBIR) Grant from the National Institute of Diabetes and Digestive and Kidney Diseases of the National Institutes of Health (NIH) in support of research on orally stable peptide antagonists of the interleukin-23 (IL-23) receptor as potential treatments for inflammatory bowel diseases. The Company recorded the eligible costs incurred under the SBIR grant as a reduction of research and development expenses and as a receivable as of March 31, 2016.

Net Loss per Share Attributable to Common Stockholders

Basic net loss per share attributable to common stockholders is calculated by dividing the net loss attributable to common stockholders by the weighted average number of shares of common stock outstanding during the period, without consideration of potentially dilutive securities. The net loss attributable to common stockholders is calculated by adjusting the net loss of the Company for the accretion on the redeemable convertible preferred stock. Diluted net loss per share attributable to common stockholders is the same as basic net loss per share attributable to common stockholders for all periods presented since the effect of potentially dilutive securities are anti-dilutive given the net loss of the Company.

Unaudited Pro Forma Net Loss per Share Attributable to Common Stockholders

The unaudited pro forma basic and diluted net loss per share attributable to common stockholders has been computed to give effect to the conversion of the shares of redeemable convertible preferred stock into common stock as if such conversion had occurred at the earlier of the beginning of the period or the date of issuance, if later. Also, the numerator in the pro forma basic and diluted net loss per share attributable to common stockholders calculation has been adjusted to remove gains or losses resulting from the remeasurement of the redeemable convertible preferred stock warrant liability as the warrants will be reclassified to additional paid-in capital. The unaudited pro forma net loss per share attributable to common stockholders does not include the shares to be sold and related proceeds to be received from the proposed initial public offering.

3. Fair Value Measurements

Financial assets and liabilities are recorded at fair value. The accounting guidance for fair value provides a framework for measuring fair value, clarifies the definition of fair value and expands disclosures regarding fair value measurements. Fair value is defined as the price that would be received to sell an asset or paid to transfer a liability (an exit price) in an orderly transaction between market participants at the reporting date. The accounting guidance establishes a three-tiered hierarchy, which prioritizes the inputs used in the valuation methodologies in measuring fair value as follows:

Level 1—Inputs are unadjusted quoted prices in active markets for identical assets or liabilities at the measurement date.

3. Fair Value Measurements (Continued)

Level 2—Inputs (other than quoted market prices included in Level 1) are either directly or indirectly observable for the asset or liability through correlation with market data at the measurement date and for the duration of the instrument's anticipated life.

Level 3—Inputs reflect management's best estimate of what market participants would use in pricing the asset or liability at the measurement date. Consideration is given to the risk inherent in the valuation technique and the risk inherent in the inputs to the model.

In determining fair value, the Company utilizes quoted market prices, broker or dealer quotation, or valuation techniques that maximize the use of observable inputs and minimize the use of unobservable inputs to the extent possible as well as considers counterparty credit risk in its assessment of fair value.

The following table presents the fair value of the Company's financial assets and liabilities determined using the inputs defined above (amounts in thousands).

	December 31, 2015			
	Level 1	Level 2	Level 3	Total
Assets:				
Money market funds(a)	$ 2,136	$ —	$ —	$ 2,136
Corporate bonds(b)	—	7,368	—	7,368
Commercial paper(b)	—	500	—	500
Total financial assets	$ 2,136	$7,868	$ —	$10,004
Liabilities:				
Redeemable convertible preferred stock tranche liability	$ —	$ —	$1,643	$ 1,643
Redeemable convertible preferred stock warrant liability	—	—	480	480
Total financial liabilities	$ —	$ —	$2,123	$ 2,123

	March 31, 2016			
	Level 1	Level 2	Level 3	Total
Assets:				
Money market funds(a)	$26,626	$ —	$ —	$26,626
Corporate bonds(b)	—	393	—	393
Total financial assets	$26,626	$ 393	$ —	$27,019
Liabilities:				
Redeemable convertible preferred stock warrant liability	$ —	$ —	$1,005	$ 1,005
Total financial liabilities	$ —	$ —	$1,005	$ 1,005

(a) Included in cash and cash equivalents
(b) Included in available-for-sale securities

3. Fair Value Measurements (Continued)

The corporate bonds and commercial paper are classified as Level 2 as they were valued based upon quoted market prices for similar instruments in active markets, quoted prices for identical or similar instruments in markets that are not active and model-based valuation techniques for which all significant inputs are observable in the market or can be corroborated by observable market data for substantially the full term of the assets.

The fair value measurements of the redeemable convertible preferred stock tranche liability and the redeemable convertible preferred stock warrant liability are based on significant inputs not observed in the market and thus represent a Level 3 measurement. Level 3 instruments are valued based on unobservable inputs that are supported by little or no market activity and reflect the Company's assumptions in measuring fair value.

The redeemable convertible preferred stock tranche liability stems from the initial sale of the Company's Series C redeemable convertible preferred stock wherein the Company was obligated to sell additional shares in subsequent closings contingent upon a majority of the stockholders of the outstanding redeemable convertible preferred stock and/or the achievement of certain development milestones. The subsequent closings were deemed to be freestanding financial instruments that were at the option of the holders. The Company estimates the fair value of this liability using a one-step binomial lattice model in combination with Option Pricing Model. The change in fair value is recognized as a gain or loss in the condensed consolidated statements of operations. See Note 9 for further discussion on the redeemable convertible preferred stock tranche liability and related valuations.

The determination of the fair value of the redeemable convertible preferred stock warrant liability is discussed in Note 7. Generally, increases or decreases in the fair value of the underlying redeemable convertible preferred stock would result in a directionally similar impact in the fair value measurement of the warrant liability.

The following table sets forth a summary of the changes in the fair value of the Company's Level 3 financial instruments as follows (in thousands):

	Three Months Ended March 31, 2016
Redeemable Convertible Preferred Stock Tranche Liability:	
Balance at December 31, 2015	$ 1,643
Change in fair value upon revaluation	4,194
Settlement of redeemable convertible preferred stock tranche liability due to issue of Series C redeemable convertible preferred shares	(5,837)
Balance at March 31, 2016	$ —

	Three Months Ended March 31, 2016
Redeemable Convertible Preferred Stock Warrant Liability:	
Balance at December 31, 2015	$ 480
Change in fair value upon revaluation	525
Balance at March 31, 2016	$1,005

4. Balance Sheet Components

Cash Equivalents and Available-for-sale Securities

Cash equivalents and available-for-sale securities consisted of the following (in thousands):

	December 31, 2015			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Money market funds	$ 2,136	$ —	$ —	$ 2,136
Corporate bonds	7,373	—	(5)	7,368
Commercial paper	500	—	—	500
Total cash equivalents and available-for-sale securities	$10,009	$ —	$ (5)	$10,004
Classified as:				
Cash equivalents				$ 2,136
Available-for-sale securities				7,868
Total cash equivalents and available-for-sale securities				$10,004

	March 31, 2016			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Money market funds	$26,626	$ —	$ —	$26,626
Corporate bonds	393	—	—	393
Total cash equivalents and available-for-sale securities	$27,019	$ —	$ —	$27,019
Classified as:				
Cash equivalents				$26,626
Available-for-sale securities				393
Total cash equivalents and available-for-sale securities				$27,019

All available-for-sale securities held as of December 31, 2015 and March 31, 2016 had contractual maturities of less than one year. There have been no significant realized gains or losses on available-for-sale securities for the periods presented.

Prepaid Expenses and Other Current Assets

Prepaid expenses and other current assets consisted of the following (in thousands):

	December 31, 2015	March 31, 2016
Prepaid manufacturing of clinical materials	$1,253	$242
Other	305	373
Prepaid expenses and other current assets	$1,558	$615

4. Balance Sheet Components (Continued)

Accrued Expenses and Other Payables

Accrued expenses and other payables consisted of the following (in thousands):

	December 31, 2015	March 31, 2016
Accrued contract research	$ 976	$1,075
Accrued employee related expenses	754	732
Accrued legal and accounting fees	64	495
Accrued expenses and other payables	85	278
Accrued expenses and other payables	$1,879	$2,580

5. Research Collaboration and License Agreement

In October 2013, the Company's former collaboration partner decided to abandon a collaboration program with the Company and, pursuant to the terms of the agreement between the Company and the former collaboration partner, the Company elected to assume the responsibility for the development and commercialization of the product. Upon the former collaboration partner's abandonment, it assigned to the Company certain intellectual property arising from the collaboration and also granted the Company an exclusive license to certain background intellectual property rights of the former collaboration partner that relate to the products assumed by the Company. Upon the nomination of PTG-300 as a development candidate, the Company owed the former collaboration partner a payment of $250,000. If the Company initiates a Phase 1 clinical trial for PTG-300, it will pay the former collaboration partner an additional $250,000. The Company has the right, but not the obligation, to further develop and commercialize the products and, if the Company successfully develops and commercializes PTG-300 without a partner, the Company will pay to the former collaboration partner up to an additional aggregate of $128.5 million for the achievement of certain development, regulatory and sales milestone events. In addition, the Company will pay to the former collaboration partner a low single digit royalty on worldwide net sales of the product until the later of ten years from the first commercial sale of the product on the expiration of the last patent covering the product. For the three months ended March 31, 2016, the Company recorded research and development expense of $250,000 under this agreement.

6. Government Grants

Research and Development Tax Incentive

The Company recognized AUD 127,000 ($100,000) and AUD 707,000 ($510,000) as a reduction of research and development expenses for the three months ended March 31, 2015 and 2016, respectively, in connection with the Research and Development Tax Incentive from Australia. As of December 31, 2015 and March 31, 2016, the research and development tax credit receivable was AUD 978,000 ($715,000) and AUD 1.7 million ($1.3 million), respectively. In March 2016, the Company received AUD 237,000 ($181,000) for overseas findings and recorded the funds as a deferred tax incentive in the accrued expenses and other payables on the condensed consolidated balance sheet due to the possibility that the funds could have to be repaid.

SBIR Grant

In September 2015, the Company was awarded a Phase 1 SBIR Grant from the National Institute of Diabetes and Digestive and Kidney Diseases of the NIH in support of research on orally stable peptide

6. Government Grants (Continued)

antagonists of the interleukin-23 receptor (IL-23R) as potential treatments for inflammatory bowel diseases (IBD). The Company recognizes contra research and development expense when costs related to the grant have been incurred and the grant funds become contractually due from NIH. The total grant award was $224,000 and is for the period from September 2015 to August 2016. The Company recorded $69,000 as a reduction of research and development expenses for the three months ended March 31, 2016. The Company recorded a receivable for $155,000 and $224,000 as of December 31, 2015 and March 31, 2016, respectively, to reflect the eligible costs incurred under the grant that are contractually due to the Company and such amounts are included in the prepaid expenses and other current assets on the condensed consolidated balance sheets.

7. Preferred Stock Warrants

In connection with the Series B redeemable convertible preferred stock financing, the Company issued warrants to purchase 4,000,000 shares of Series B redeemable convertible preferred stock at an exercise price of $0.01 per share. These warrants will become exercisable only when certain milestones are met on programs begun as a result of collaborations entered into in 2011 and 2012. In particular, 50% of the warrants are exercisable upon the Company publicly announcing its first Investigational New Drug (IND) candidate to the extent such IND candidate is a result of, or related to, the Company's previous collaboration(s) with Ironwood Pharmaceuticals and/or Zealand Pharma A/S, and the balance are exercisable upon the first dosing of a human patient in a clinical trial that is a result of, or related to, the Company's previous collaboration(s) with Ironwood Pharmaceuticals and/or Zealand Pharma A/S. In August 2013, the initial closing date for the Series B financing, the Company issued 2,000,000 of the warrants (First Tranche Warrants). On August 15, 2014, in connection with the closing of the Series B second tranche financing, the Company issued the balance of the warrants (Second Tranche Warrants).

The fair value of the warrants outstanding as of December 31, 2015 was remeasured at $480,000, determined using a one-step binomial lattice model in combination with the Option Pricing Model and the following assumptions: risk-free interest rate of 0.90%, expected life of 1.6 years and expected volatility of 57.0% and probability of exercisability of 95% and 0% for first tranche and second tranche, respectively.

The fair value of the warrants outstanding as of March 31, 2016 was remeasured at $1.0 million, determined using a hybrid method of the Option Pricing Model with a 67% weighted value per share and the PWERM with a 33% weighted value per share. The following assumptions were used in the Option Pricing Model: risk-free interest rate of 0.73%, expected life of 2.0 years and expected volatility of 52.0%. The PWERM method included probabilities of three IPO scenarios occurring in July 2016. The scenarios were weighted based on the Company's estimate of each event occurring in deriving the estimated fair value.

The Company recorded charges of $9,000 and $525,000 for the three months ended March 31, 2015 and 2016, respectively, representing the change in the fair value of the redeemable convertible preferred stock warrant liability in the condensed consolidated statements of operations.

In March 2016, the Company made a public announcement related to a preclinical candidate which triggered the achievement of the milestone and warrants to purchase 2,000,000 shares of Series B redeemable convertible preferred stock became exercisable as of that date. In April 2016, 1,999,998 shares of Series B redeemable convertible preferred stock were issued for cash proceeds of $20,000 in connection with the exercise of warrants.

As of March 31, 2016, the milestone for the Second Tranche Warrants was not met and the outstanding warrants expired on May 10, 2016.

8. Redeemable Convertible Preferred Stock

The table below provides information on the Company's redeemable convertible preferred stock as of December 31, 2015 (in thousands, except shares and original issue price):

	Original Issue Price	Shares: Authorized	Shares: Issued and Outstanding	Carrying Value	Aggregate Liquidation Preference
Series A	$1.00	6,037,500	6,037,500	$ 1,751	$ 6,038
Series B	$0.50	40,000,000	36,000,000	18,825	18,000
Series C	$0.4979	80,337,411	35,147,617	16,420	17,500
Total redeemable convertible preferred stock		126,374,911	77,185,117	$36,996	$41,538

In March 2016, the Company completed the closing of the Series C Second Tranche and issued 45,189,794 shares of Series C redeemable convertible preferred stock for net cash proceeds of $22.5 million. The table below provides information on the Company's redeemable convertible preferred stock as of March 31, 2016 (in thousands, except shares and original issue price):

	Original Issue Price	Shares: Authorized	Shares: Issued and Outstanding	Carrying Value	Aggregate Liquidation Preference
Series A	$1.00	6,037,500	6,037,500	$ 1,751	$ 6,038
Series B	$0.50	40,000,000	36,000,000	18,825	18,000
Series C	$0.4979	80,337,411	80,337,411	44,785	40,000
Total redeemable convertible preferred stock		126,374,911	122,374,911	$65,361	$64,038

The Company recorded zero and $40,000 for the accretion of the redeemable convertible preferred stock during the three months ended March 31, 2015 and 2016, respectively. The accretion was recorded as an offset to the additional paid-in capital.

9. Redeemable Convertible Preferred Stock Tranche Liability

In July 2015, the Company entered into the Series C Preferred Stock Purchase Agreement (the Series C Agreement) for the issuance of up to 80,337,411 shares of Series C redeemable convertible preferred stock at a price of $0.4979 per share, in multiple closings. The initial closing occurred on July 10, 2015, whereby 35,147,617 shares of Series C redeemable convertible preferred stock were issued for gross proceeds of approximately $17.5 million. According to the initial terms of the Series C Agreement, the Company could issue 45,189,794 additional shares under the same terms as the initial closing, in a subsequent closing (Series C Second Tranche) contingent upon the achievement of certain development milestones.

On the date of the initial closing, the Company recorded a Series C redeemable convertible preferred stock liability of $1.0 million, as the fair value of the obligation/right to complete the Series C Second Tranche. The fair value of the Series C redeemable convertible preferred stock liability on the date of the initial closing was determined using a one-step binomial lattice model in combination with the option pricing method based on the

9. Redeemable Convertible Preferred Stock Tranche Liability (Continued)

following assumptions: 90% probability of achievement of the development milestones, stock price of $0.4979 per share, expected term of 1.0 year, and risk-free rate of 0.5%.

At December 31, 2015, the fair value of the Series C redeemable convertible preferred stock liability was remeasured and determined to be $1.6 million using a one-step binomial lattice model in combination with the option pricing model based on the following assumptions: 95% probability of achievement of the development milestones, stock price of $0.4979 per share, expected term of 0.53 year, and risk-free rate of 0.9%.

In March 2016, the Company completed the closing of the Series C Second Tranche and issued 45,189,794 shares of Series C redeemable convertible preferred stock for net cash proceeds of $22.5 million. At this time the Series C redeemable convertible preferred stock liability was remeasured at $5.8 million, determined using a hybrid method of the Option Pricing Model with a 67% weighted value per share and the PWERM with a 33% weighted value per share. The following assumptions were used in the Option Pricing Model: risk-free interest rate of 0.73%, expected life of 2.0 years and expected volatility of 52.0%. The PWERM method included probabilities of three IPO scenarios occurring in July 2016. The scenarios were weighted based on the Company's estimate of each event occurring in deriving the estimated fair value. Upon the closing of the Series C Second Tranche, the Series C redeemable convertible preferred stock liability was terminated and the balance of the liability of $5.8 million was reclassified to redeemable convertible preferred stock.

For the three months ended March 31, 2015 and 2016, the Company recorded a charge of zero and $4.2 million, respectively, for the change in the fair value of the Series C redeemable convertible preferred stock liability in the condensed consolidated statements of operations.

10. Common Stock

The Company had reserved shares of common stock for issuance, on an as-converted basis, as follows:

	December 31, 2015	March 31, 2016
Redeemable convertible preferred stock outstanding	5,323,103	8,439,641
Options issued and outstanding	833,178	783,341
Options available for future grants	147,219	635,530
Redeemable convertible preferred stock warrants	275,861	275,861
Total	6,579,361	10,134,373

11. Stock Option Plan

As of March 31, 2016, the Company has reserved 1,578,365 shares of common stock for issuance under the 2007 Stock Option Plan.

11. Stock Option Plan (Continued)

Activity under the Company's stock option plan is set forth below:

	Options Available for Grant	Options Outstanding	Options Outstanding: Weighted-Average Exercise Price Per Share	Options Outstanding: Weighted-Average Remaining Contractual Life (years)	Options Outstanding: Aggregate Intrinsic Value
					(in thousands)
Balances at December 31, 2015	147,219	833,178	$1.33	8.56	
Additional options authorized	549,977	—			
Options granted	(61,666)	61,666	1.16		
Options exercised	—	(111,503)	1.28		
Balances at March 31, 2016	635,530	783,341	1.32	8.44	$2,259
Options exercisable—March 31, 2016		172,236	1.35	6.45	$ 492
Options vested and expected to vest—March 31, 2016		772,073	1.32	8.43	$2,226

The aggregate intrinsic values of options outstanding, exercisable, vested and expected to vest were calculated as the difference between the exercise price of the options and the fair value of the Company's common stock, as determined by the Company's Board of Directors, as of March 31, 2016.

During the three months ended March 31, 2015 and 2016, the estimated weighted-average grant-date fair value of common stock underlying options granted was $1.04 and $0.68 per share, respectively.

Employee Stock Options Valuation

The fair value of employee and director stock option awards was estimated at the date of grant using a Black-Scholes option-pricing model with the following assumptions:

	Three Months Ended March 31,	
	2015	2016
Expected term (in years)	5.89	5.94
Expected volatility	59.8%	64.8%
Risk-free interest rate	1.57%	1.27%
Dividend yield	—	—

11. Stock Option Plan (Continued)

Stock Options Granted to Non-employees

Stock-based compensation related to stock options granted to non-employees is recognized as the stock options are earned.

During the three months ended March 31, 2015, and 2016, the Company recorded stock-based compensation expense of $5,000 and $20,000, respectively, related to non-employee consultants.

Stock-Based Compensation

Total stock-based compensation expense recognized for both employees and non-employees was as follows (in thousands):

	Three Months Ended March 31,	
	2015	2016
Research and development	$ 8	$29
General and administrative	11	27
Total stock-based compensation expense	$19	$56

As of March 31, 2016 there was $436,000 of total unrecognized stock-based compensation costs that the Company expects to recognize over a period of approximately 3.0 years.

12. Net Loss per Share Attributable to Common Stockholders and Pro Forma Net Loss per Share Attributable to Common Stockholders

As the Company had net losses for the three months ended March 31, 2015 and 2016, all potential common shares were determined to be anti-dilutive. The following table sets forth the computation of the basic and diluted net loss per share attributable to common stockholders during the three months ended March 31, 2015 and 2016 (in thousands, except share and per share data):

	Three Months Ended March 31,	
	2015	2016
Numerator:		
Net loss	$ (2,697)	$ (11,747)
Accretion of redeemable convertible preferred stock	—	(40)
Net loss attributable to common stockholders	$ (2,697)	$ (11,787)
Denominator:		
Weighted-average shares used to compute net loss per common share, basic and diluted	229,483	287,800
Net loss per share attributable to common stockholders, basic and diluted	$ (11.75)	$ (40.96)

12. Net Loss per Share Attributable to Common Stockholders and Pro Forma Net Loss per Share Attributable to Common Stockholders (Continued)

The following outstanding shares of potentially dilutive securities have been excluded from diluted net loss per share calculations for the three months ended March 31, 2015 and 2016, because their inclusion would be anti-dilutive:

	Three Months Ended March 31,	
	2015	2016
Redeemable convertible preferred stock on an as-converted basis	2,899,134	8,439,641
Options to purchase common stock	510,959	783,341
Warrants to purchase redeemable convertible preferred stock on an as-converted basis	275,861	275,861
Total	3,685,954	9,498,843

Pro Forma Net Loss per Share Attributable to Common Stockholders

The following table sets forth (in thousands, except share and per share amounts) the computation of the Company's unaudited pro forma basic and diluted net loss per share attributable to common stockholders after giving effect to the automatic conversion of redeemable convertible preferred stock using the as-if converted method into common stock as though the conversion had occurred at the beginning of the period presented or date of issuance, if later. The numerator in the pro forma basic and diluted net loss per common share calculation has been adjusted to remove gains or losses resulting from the remeasurement of the redeemable convertible preferred stock warrant liability as the warrants will become warrants to purchase common stock and will be reclassified to additional paid-in capital upon the completion of the initial public offering.

	Three Months Ended March 31, 2016
Net loss	$ (11,747)
Change in fair value of redeemable convertible preferred stock warrant liability	525
Net loss used in computing pro forma net loss per common share, basic and diluted	$ (11,222)
Weighted average shares used to compute net loss per share attributable to common stock holders, basic and diluted	287,800
Pro forma adjustment to reflect assumed conversion of redeemable convertible preferred stock	5,597,092
Shares used to compute pro forma net loss per share attributable to common stockholders, basic and diluted	5,884,892
Pro forma net loss per share attributable to common stockholders, basic and diluted	$ (1.91)

13. Subsequent Events

In April 2016, 1,999,998 shares of Series B redeemable convertible preferred stock were issued in connection with the exercise of warrants for cash proceeds of $20,000.

In April 2016, the Company entered into an amendment to its facility lease agreement to increase the leased space in Milpitas, California. Under the amended lease agreement, the Company will make additional lease payments of $80,000 through April 2018.

In May 2016, the remaining warrants for the purchase of 2,000,000 shares of Series B redeemable convertible preferred stock expired unexercised.

In July 2016, the Company was awarded a Phase 1 Small Business Innovation Research (SBIR) Grant for $219,000 from the National Institute of Heart and Lung Diseases of the National Institutes of Health in support of preclinical research aimed at discovering and optimizing lead molecules as novel peptide mimetics of the natural hepcidin hormone.

In July 2016, the Company's board of directors approved an amendment to the Company's amended and restated certificate of incorporation to effect a reverse split of the Company's issued and outstanding common stock at a 14.5-for-1 ratio, which was effected on August 1, 2016. The par value and authorized shares of common stock and convertible preferred stock were not adjusted as a result of the reverse split. All issued and outstanding common stock, options to purchase common stock and per share amounts contained in the financial statements have been retroactively adjusted to reflect the reverse stock split for all periods presented. The financial statements have also been retroactively adjusted to reflect a proportional adjustment to the conversion ratio for each series of preferred stock that will be effected in connection with the reverse stock split.

The Company has reviewed and evaluated subsequent events through August 1, 2016, the date the unaudited condensed consolidated financial statements were available for issuance.

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5,835,000

SHARES OF COMMON STOCK

Leerink Partners **Barclays** **BMO Capital Markets**

Until , 2016 (25 days after the commencement of this offering), all dealers that buy, sell or trade shares of our common stock, whether or not participating in this offering, may be required to deliver a prospectus. This delivery requirement is in addition to the obligation of dealers to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.