Table of Contents

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2017

or

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from to
Commission File No. 001-37852

PROTAGONIST THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**98-0505495**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
7700 Gateway Boulevard, Suite 140 Newark, California 94560	**(510) 474-0170**
(Address, including zip code, of registrant's principal executive offices)	**(Telephone number, including area code, of registrant's principal executive offices)**

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Name of each exchange on which registered**
Common Stock, $0.00001 par value	**The Nasdaq Global Market**

Securities registered pursuant to Section 12(g) of the Act:
None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☐ No ☒

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ☐ No ☒

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes ☒ No ☐

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation SK (§ 229.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10K or any amendment to this Form 10K. Yes ☐ No ☒

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	☐	Accelerated filer	☒
Non-accelerated filer	☐ (Do not check if a smaller reporting company)	Smaller reporting company	☐
		Emerging growth company	☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. Yes ☒ No ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act of 1934). Yes ☐ No ☒

The aggregate market value of the voting stock held by non-affiliates of the registrant was approximately $109.6 million as of June 30, 2017, based upon the closing sale price on The Nasdaq Global Market reported on June 30, 2017. Excludes an aggregate of 7,209,737 shares of the registrant's common stock held by officers, directors and affiliated stockholders. For purposes of determining whether a stockholder was an affiliate of the registrant at June 30, 2017, the registrant assumed that a stockholder was an affiliate of the registrant at June 30, 2017 if such stockholder (i) beneficially owned 10% or more of the registrant's common stock, as determined based on public filings and/or (ii) was an executive officer or director or was affiliated with an executive officer or director of the registrant at June 30, 2017. Exclusion of such shares should not be construed to indicate that any such person possesses the power, direct or indirect, to direct or cause the direction of the management or policies of the registrant or that such person is controlled by or under common control with the registrant.

There were 21,103,775 shares of registrant's Common Stock, par value $0.00001 per share, outstanding as of February 28, 2018.

DOCUMENTS INCORPORATED BY REFERENCE:

Portions of the registrant's definitive Proxy Statement for the registrant's 2018 Annual Meeting of Stockholders, to be filed subsequent to the date hereof with the Securities and Exchange Commission (SEC), are incorporated by reference into Part III of this report. Such proxy statement will be filed with the SEC not later than 120 days after the end of the registrant's fiscal year ended December 31, 2017.

PROTAGONIST THERAPEUTICS, INC.
2017 FORM 10-K ANNUAL REPORT
TABLE OF CONTENTS

PART I

Statements made in this Annual Report on Form 10-K contain certain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. Forward-looking statements are identified by words such as "believe," "will," "may," "estimate," "continue," "anticipate," "intend," "should," "plan," "expect," "predict," "could," "potentially" or the negative of these terms or similar expressions. You should read these statements carefully because they discuss future expectations, contain projections of future results of operations or financial condition, or state other "forward-looking" information. These statements relate to our future plans, objectives, expectations, intentions and financial performance and the assumptions that underlie these statements. These forward-looking statements are subject to certain risks and uncertainties that could cause actual results to differ materially from those anticipated in the forward-looking statements. Factors that might cause such a difference include, but are not limited to, those discussed in this report in "Item 1A. Risk Factors" and elsewhere in this Annual Report. In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this report, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and investors are cautioned not to unduly rely upon these statements. Forward-looking statements are based on our management's beliefs and assumptions and on information currently available to our management. These statements, like all statements in this report, speak only as of their date, and we undertake no obligation to update or revise these statements in light of future developments. We caution investors that our business and financial performance are subject to substantial risks and uncertainties.

Item 1. Business.

We are a clinical-stage biopharmaceutical company with a proprietary technology platform that enables the discovery and development of novel constrained peptide-based drug candidates that address significant unmet medical needs. Our product candidates are designed to affect critical steps in the biological pathways of particular diseases, for example, by blocking protein-protein interactions ("PPI's"). We believe our peptide-based approach has advantages over alternative approaches such as small molecules and antibodies. Two of our clinical stage product candidates, PTG-100 and PTG-200, are potential first-in-class oral drugs that block biological pathways currently targeted by marketed injectable antibody drugs and offer targeted delivery to the gastrointestinal ("GI") tissue compartment. We believe that, as compared to antibody drugs, these product candidates have the potential to provide improved safety due to minimal exposure in the blood, increased convenience and compliance due to oral delivery, and the opportunity for the earlier introduction of targeted therapy. As a result, if approved, they may transform the existing treatment paradigm for inflammatory bowel disease ("IBD"), a GI disease consisting primarily of ulcerative colitis ("UC"), and Crohn's disease ("CD"). Our third clinical stage product candidate, PTG-300, mimics the effect of the hormone hepcidin and has the potential to treat the anemia caused by certain rare blood disorders.

Peptide therapeutics represent a substantial and growing therapeutic class with more than 60 U.S. Food and Drug Administration ("FDA") approved drugs. Our platform enables us to discover novel, structurally constrained peptides that retain certain key advantages of both oral small molecules 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 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.

PTG-100, a potential first-in-class oral, alpha-4-beta-7 ("α4β7") integrin antagonist, is currently in a global Phase 2b clinical trial for the treatment of moderate-to-severe UC that is anticipated to randomize approximately 240 patients at approximately 100 clinical sites. We anticipate conducting an interim futility analysis in the first quarter of 2018 and reporting top-line results in the fourth quarter of 2018. If this trial is successful, we anticipate conducting end-of-Phase 2 meetings with global health authorities and initiating pivotal clinical development programs in both UC and CD in 2019.

We also anticipate developing PTG-100 for the treatment of chronic pouchitis, a GI condition that occurs in many post-surgical IBD patients. We have completed a pre-Investigational New Drug ("IND") meeting with the FDA regarding the development pathway for PTG-100 in this indication and anticipate proceeding with clinical development activities pending a successful outcome of the Phase 2b futility analysis.

PTG-200 is a potential first-in-class oral Interleukin-23 receptor ("IL-23R") antagonist for the treatment of IBD. It is currently in a Phase 1 healthy volunteer clinical study that was initiated in the fourth quarter of 2017. We have entered into a worldwide license and collaboration agreement with Janssen Biotech, Inc. ("Janssen"), a Johnson and Johnson company, to co-develop and co-detail PTG-200 for all indications, including IBD. See "Item 7. Management's Discussion and Analysis – Overview" and Note 3 to the Consolidated Financial Statements included elsewhere in this Annual Report on Form 10-K for additional information.

Our novel peptides have potential applicability in a wide range of therapeutic areas in addition to GI diseases. Our third product candidate, PTG-300, is a mimic of the hormone hepcidin that we are developing for the treatment of anemia in certain rare blood disorders, with an initial focus on beta-thalassemia. In the fourth quarter of 2017, we completed a successful Phase 1 study of PTG-300 in healthy volunteers which established pharmaceutical proof of concept. In 2018, we anticipate filing an IND in the United States and related clinical trial applications outside the United States and initiating a Phase 2 study of PTG-300 in patients with beta-thalassemia. PTG-300 has received an orphan drug designation from the FDA for the treatment of beta-thalassemia.

In addition, we continue to use our peptide technology platform to discover product candidates against targets in disease areas with significant unmet medical needs. In 2018, we anticipate initiating IND-enabling studies for a fourth product candidate, an oral peptide targeting a GI condition other than IBD.

Our Product Candidates

PTG-100

PTG-100 has the potential to be a first in class oral, α4β7 antagonist for the treatment of IBD. The α4β7 integrin is 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 pharmacodynamic ("PD") biomarker assays similar to those described in scientific publications as used with Entyvio® and other antibodies as indicators of target engagement to establish proof-of-concept ("POC") in our Phase 1 clinical trial with PTG-100. These PD data include dose dependent 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 the 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, each of which evaluated safety, pharmacokinetics ("PK"), and PD-based POC in healthy subjects. The Phase 1 clinical trial was completed in June 2016. Dose escalation proceeded up to 1,000 mg in both single and multiple dosing. There were no serious adverse events reported in the 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 received placebo.

We initiated a global Phase 2b randomized, double-blinded, placebo-controlled dose-finding clinical trial in the fourth quarter of 2016 to assess the safety and efficacy of PTG-100 in moderate-to-severe UC patients. We anticipate that the trial will enroll approximately 240 subjects at approximately 100 sites in the United States, Canada, Europe (Western, Central, and Eastern), Asia, Australia, and New Zealand. The primary objectives of our Phase 2b clinical trial are to evaluate the safety and tolerability of PTG-100 and its efficacy 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 pharmacodynamic responses, and to evaluate any immunogenicity over 12 weeks. The trial will include subjects who have had prior exposure to tumor necrosis factor-alpha ("TNF-α") inhibitors and subjects who have not been treated with biologics. Subjects will be randomized to one of four dose arms (150mg/300mg/900mg PTG-100 or placebo) for 12 weeks of once-daily oral dosing, followed by four weeks of safety follow-up. An interim futility analysis is expected to be performed in the first quarter of 2018, and if futility criteria are not met, one or two PTG-100 doses will be selected for continued randomization of the remaining subjects. We expect to complete the study and report top-line data in the fourth quarter of 2018. We expect that this trial will support end-of-Phase 2 meetings with global health authorities and enable the initiation of a Phase 3 pivotal program.

The primary endpoints are consistent with those used in the clinical development of previously approved drugs for UC. The trial is 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. The evaluation of clinical remission is based on the Mayo Score, which is a well-established composite assessment that utilizes patient-reported outcomes and endoscopic improvement. Secondary efficacy endpoints will include endoscopic response, clinical response, endoscopic remission, change in endoscopic subscore, change in stool frequency and rectal bleeding subscores, change in fecal calprotectin, change in the IBD questionnaire, change in Mayo score and change in partial Mayo score, from baseline to multiple points during the induction period.

We plan to develop PTG-100 initially for the treatment of moderate-to-severe UC and CD, as well as chronic pouchitis. Subsequent indications may include mild-to-moderate UC, 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. Interleukin-23 ("IL-23"), a member of the IL-12 family of pro-inflammatory cytokines, is a protein that regulates inflammatory and immune function and plays 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, psoriatic arthritis, and moderate-to-severe CD.

We have completed pre-clinical POC studies and IND-enabling studies for PTG-200, and we initiated a Phase 1 clinical trial in the fourth quarter of 2017. The Phase 1 study, which is being conducted in Australia, is a randomized, double-blind, placebo-controlled, single and multiple dose-escalation trial in approximately eighty healthy volunteers. Secondary endpoints include the identification of the maximally tolerated dose and the evaluation of pharmacokinetic parameters.

We have a worldwide license and collaboration agreement with Janssen to co-develop and co-detail PTG-200 for all indications as described in Item 7. "Management's Discussion and Analysis – Overview" and Note 3 to the Consolidated Financial Statements included elsewhere in this Annual Report on Form 10-K. We and Janssen currently plan to develop PTG-200 initially for the treatment of moderate-to-severe CD, potentially followed by UC.

PTG-300

PTG-300 is an injectable peptide that mimics the effect of the hormone hepcidin. We are developing PTG-300 for the treatment the chronic anemia that arises from insufficient red blood cell production, known as ineffective erythropoiesis, in certain rare blood disorders, including beta-thalassemia. In these diseases, excessive quantities of iron

in the bone marrow inhibit the production of red blood cells causing anemia. In healthy individuals, hepcidin regulates iron levels by inhibiting iron absorption from the GI tract and by limiting macrophage release of iron in the bone marrow. Individuals with beta-thalassemia and MDS often have insufficient hepcidin to maintain appropriate iron levels. Because of stability issues, complexity of synthesis and solubility limitations, direct hepcidin replacement is not a practical therapeutic approach. We developed PTG-300 as a stable, soluble, manufacturable hepcidin mimetic that could potentially prevent excessive iron accumulation and iron toxicity with weekly sub-cutaneous injections.

We completed IND-enabling studies during the first half of 2017 and completed a Phase 1 clinical trial during the fourth quarter of 2017. The Phase 1 study demonstrated that PTG-300 induces dose-related reductions in serum iron, which persist beyond 72 hours at higher dose levels. In the study PTG-300 produced dose-dependent increases in blood exposure and was well tolerated, with no serious adverse events or dose-limiting toxicities.

In 2018, we anticipate filing an IND in the United States and related clinical trial applications outside the United States and initiating a Phase 2 study of PTG-300 in patients with beta-thalassemia. PTG-300 has received orphan designation from the FDA for the treatment of beta-thalassemia.

Additional Product Candidates

We are currently researching potential oral and injectable peptide-based product candidates for a range of conditions including, but not restricted to, GI diseases. In 2018, we anticipate initiating IND-enabling studies for a fourth product candidate, an oral peptide targeting a GI condition other than IBD.

The Evolution of Antibody Drugs for Targeted Therapy and Their Limitations

Before 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 often not capable of affecting the critical processes involved in diseases, for example by blocking protein-protein interactions ("PPIs") or by mimicking naturally occurring molecules. 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.

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

- *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 anti-drug antibodies ("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.

- *Injections or infusions are associated with significant patient burden.* Antibody drugs are large proteins that are not stable when orally administered. As a consequence, antibody based therapies are administered primarily by injection or infusion into systemic circulation even when the target of the antibody is a specific site in the body. 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

Our Therapeutics Platform

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 selective and potent peptides that may be orally delivered if desired. The well-folded conformation in our constrained peptides is typically derived by disulfide bonds, a structural feature inherent in many naturally occurring peptides.

Our IBD Solution: Oral, GI-Restricted Peptides as Targeted Therapies

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, 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.

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. These chronic diseases tend to run in families and they affect males and females equally. 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 under the age of 20.

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 2015, GlobalData estimated that the UC market reached approximately $4.8 billion across seven major markets: the United States, France, Germany, Italy, Spain, the United Kingdom and Japan. By the end of 2025, the UC market is expected to reach $5.5 billion, reflecting a compound annual growth rate of 1.3%. In 2016, GlobalData estimated that the CD market reached approximately $9.2 billion across those same seven major markets. By the end of 2026, the CD market is expected to reach $13.4 billion, representing a compound annual growth rate of 3.8%.

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. In 2016, Stelara®, a subcutaneously administered antibody that targets the IL-23 and IL-12 cytokines, was approved for the treatment of adult patients with moderate to severe active CD wo had failed to respond to, or were intolerant of, standard therapies or a TNF-α antibody.

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.

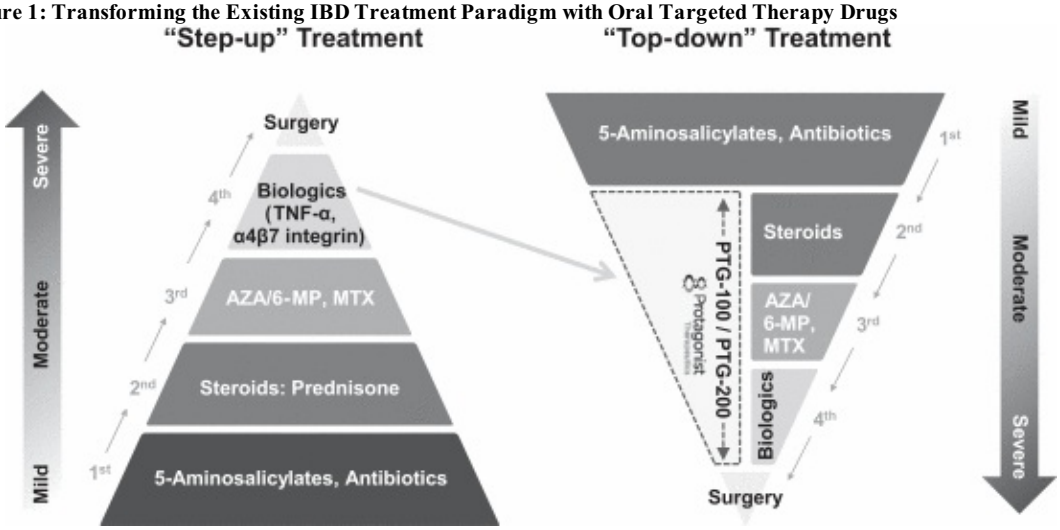
The Evolving IBD Treatment Paradigm

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. As a result, only a portion of IBD patients currently receive a targeted antibody therapy.

For moderate-to-severe IBD patients, physicians may prescribe TNF-α antibody drugs, Entyvio®, or, in the case of CD, Stelara®, 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% resulting in a greater need for hospitalization.

We believe the development of new, potent and targeted therapies for IBD with oral delivery may offer more effective treatment options for moderate-to-severe IBD patients. In addition, many clinicians are already advocating for an earlier introduction of targeted therapeutics in IBD to reduce, replace or delay the use of corticosteroids and non-specific oral immunomodulators. This treatment approach is often referred to as a "top-down" approach as therapeutics that are currently at the top of the "step-up" pyramid are moved down to earlier in the treatment paradigm (see Figure 1). We believe we are well-positioned to be leaders in this 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 and have the potential to offer improved patient safety, improved compliance and convenience and reduced immunogenicity as compared to antibody drugs. In addition, key opinion leaders are increasingly viewing the a4β7 integrin antagonist Entyvio® as a preferable alternative to TNF-α blockers for the treatment of IBD due to its improved safety profile. Taken together, we believe that these trends may result in our product candidates, if approved, being used more broadly than antibody drugs in moderate-to-severe IBD patients and potentially being used for the treatment of mild-to-moderate disease.

Figure 1: 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 and Rationale

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 a4β7 integrin to MAdCAM-1, PTG-100 may prevent T cells from entering the GI tissue compartment, thereby reducing the 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 utilized similar PD-based POC 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 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 were 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. 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") and were similarly evaluated in normal healthy volunteers in our Phase 1 clinical trial. These blood PD responses demonstrated that PTG-100 engaged its intended α4β7 target and helped guide human dosing for our Phase 2b clinical trial.

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 assays ("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. PTG-100 exhibited greater than a 100,000-fold selectivity against other structurally similar integrins, α4β*1* and αLβ2, in cell adhesion assays which is comparable to the selectivity of vedolizumab. 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 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.

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. Further, PTG-100 has an oral systemic bioavailability of less than 0.5%.

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 2). 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.

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 and multiple doses and decreases in RE after multiple doses in healthy mice and colitis

mice. 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.

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 and 12 weeks 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 chronic GLP toxicology studies to support our anticipated Phase 3 program.

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 is being 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.

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. 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. 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.

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.

Establishing Pharmacodynamic POC in Humans

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

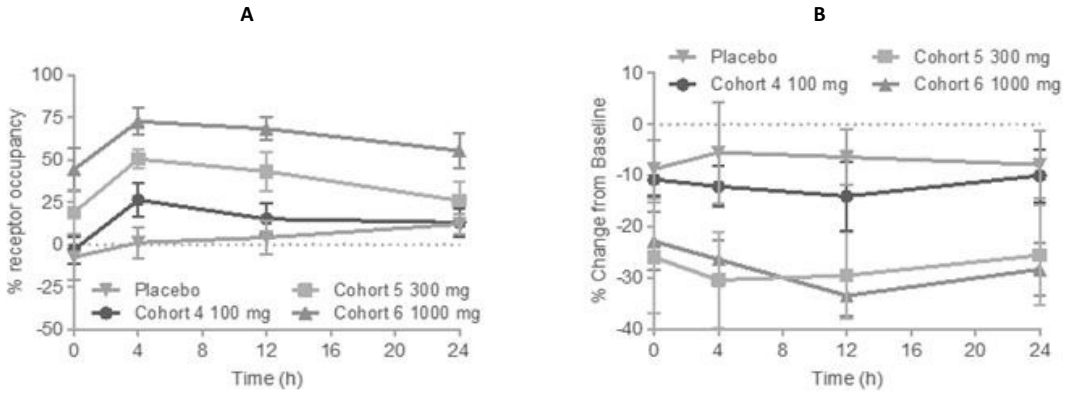
treatment groups were significant compared to placebo at 100 mg ($p<0.0005$), 300 mg ($p<0.0001$) and 1,000 mg ($p<0.0001$) four hours post dose on Day 14 (Figure 2A).

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. For α4β7, downregulation of expression was significant in treatment groups, compared to placebo at 300 mg and 1,000 mg ($p<0.01$) (Figure 2B).

The single dose 300 mg cohort was evaluated under fasted and fed (standard high fat diet) conditions. Blood drug levels and blood RO 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.

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.

Figure 2: (A) Percent Receptor Occupancy and (B) Receptor Expression of α4β7 on CD4+ Memory T Cells in Blood of Healthy Humans Dosed for 14 Days



Establishing Pharmacodynamic POC in Humans

Data from our mouse colitis studies support our conclusion that blood RO is a correlate of target engagement in the GI tissue compartment in the dose ranges studied. In our Phase 1 clinical trial, blood RO on CD4+ memory α4β7+T cells increased in a dose-dependent and time-dependent manner. For receptor occupancy in the SAD cohorts, treatment groups were significant compared to placebo at 100 mg ($p<0.05$), 300 mg ($p<0.005$) and 1,000 mg ($p<0.0001$). In the MAD cohorts, 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 (Figure 2A).

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. For α4β7, downregulation of expression was significant in treatment groups, compared to placebo at 300 mg and 1,000 mg ($p<0.01$) (Figure 2B).

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.

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.

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 IL-23R and specifically 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. 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 receptor 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 have implicated IL-23R mutations as a risk factor associated with susceptibility to IBD. The antagonist infused antibody drug ustekinumab (marketed as Stelara® for psoriasis, psoriatic arthritis, and moderate-to-severe CD) is a p40 antagonist antibody that inhibits both the IL-23 and IL-12 pathways. Next-generation IBD antibody drugs, such as guselkumab, target the p19 subunit of the IL-23 ligand and are specific to the IL-23 pathway, which is believed to be an important driver of IBD pathology, while not blockading the IL-12 pathway. IL-12 is believed to be important in immune surveillance against the development of infections and malignancies.

We believe that the oral, GI-restricted nature of PTG-200 will allow PTG-200 to be a potent inhibitor of the IL-23 pathway 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.

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

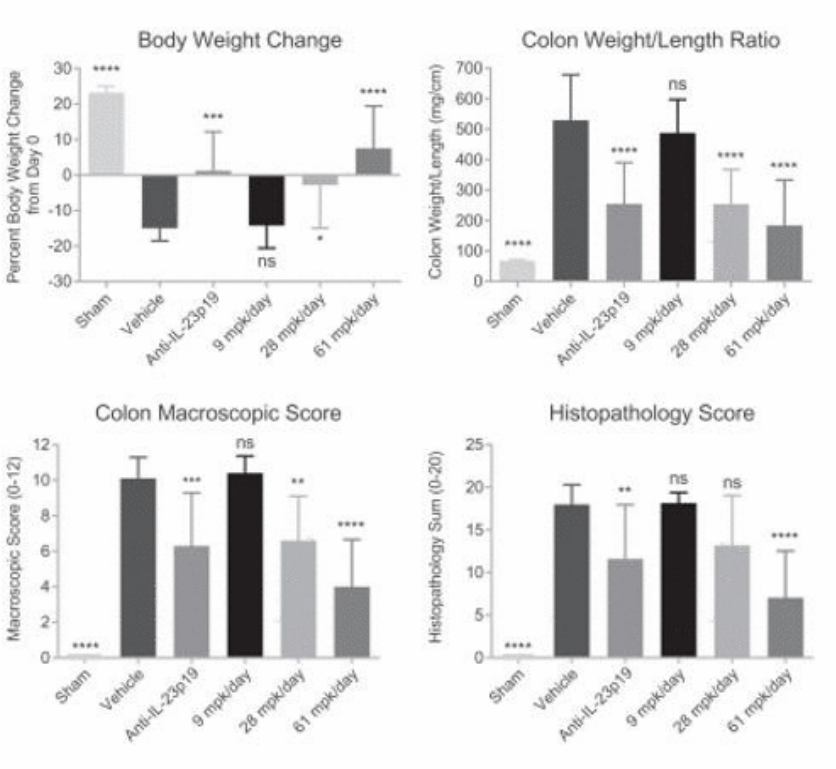
PTG-200 potently inhibited binding of IL-23 to the IL-23 receptor in several biochemical (ELISA) and cell (transformed and primary) signaling assays in a subnanomolar to low nanomolar concentration range sufficient to inhibit 50% of binding. PTG-200 exhibited greater than a 50,000-fold selectivity against other structurally similar receptors (IL-12Rb1 and IL-6R) thereby potentially reducing the risk of off target interactions. In total, these drug properties provide evidence to characterize PTG-200 as a potential first-in-class orally stable IL-23R-specific antagonist.

In PK studies in rats and cyno, 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. Similar results were observed in cyno.

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 in a dose dependent manner (Figure 3). 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 pro-inflammatory IL-23 induced cytokines in the colon and the IBD disease biomarker lipocalin (LCN2) in the serum and feces.

Figure 3: 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 injected and therefore 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 Pre-Clinical Safety Studies

In pre-clinical safety and toxicity studies in rats, PTG-200 was well-tolerated with no adverse events at the highest dose level tested.

Clinical Development Plans

We initiated a Phase 1 clinical trial of PTG-200 in the fourth quarter of 2017 to evaluate safety, tolerability, and PK. Assuming successful completion of this study, we anticipate the next step in clinical development will be a randomized, double-blind, placebo-controlled Phase 2 POC clinical trial in patients with moderate-to-severe CD. We are developing PTG-200 in collaboration with Janssen. See Item 7. "Management's Discussion and Analysis – Overview"

and Note 3 to the Consolidated Financial Statements included elsewhere in this Annual Report on Form 10-K for additional information.

PTG-300: AN INJECTABLE HEPCIDIN MIMETIC

PTG-300 was discovered through our peptide technology platform and is being developed as a novel mimetic of the hormone hepcidin to potentially treat anemia due to ineffective erythropoiesis in certain rare blood disorders with an initial focus on beta-thalassemia. In these diseases, excessive quantities of iron in the bone marrow inhibit the production of red blood cells, causing anemia. In healthy individuals, hepcidin regulates iron levels in the serum and the bone marrow. Because of stability issues complexity of synthesis and solubility limitations, direct hepcidin replacement is not a practical therapeutic approach. We designed PTG-300 as a stable, soluble, manufacturable hepcidin mimetic that can treat anemia with weekly or less frequent subcutaneous delivery.

Mechanism of Action and Rationale

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. By binding to the extracellular domain of ferroportin, hepcidin prevents the release of iron from cells. It can thus inhibit iron absorption from the GI tract by interacting with duodenal enterocytes and limit the release of iron in the bone marrow by interacting with macrophages. Excessive quantities of iron in the bone marrow induce ineffective erythropoiesis resulting in anemia. By mimicking hepcidin, PTG-300 may restore normal levels of iron in the bone marrow allowing for sufficient production of red blood cells. In addition, by limiting the release of iron into the blood, PTG-300 may inhibit the damage caused by excessive absorption of iron by vital organs.

Overview of Beta-Thalassemia and Current Therapies

We anticipate our initial clinical indication for PTG-300 will be the treatment of anemia in beta-thalassemia. Beta-thalassemia patients frequently have elevated levels of iron in the blood serum and in the bone marrow. Elevated levels of iron in the serum can cause damage to vital organs in the form of cardiomyopathy or liver fibrosis and can make the patient more vulnerable to infections. In the bone marrow, elevated levels of iron can prevent red blood cells from fully developing, resulting in anemia. In addition, the resulting immature red blood cells can aggregate in the spleen and enlarge it to such an extent that it must be surgically removed. The elevated iron levels seen in beta-thalassemia patients are often caused by disease-related suppression of hepcidin production.

Existing treatment options for hepcidin related anemia and iron overload are limited. Erythropoietic-stimulating agents, such as erythropoietin, are commonly used. However, these agents are often insufficient to treat the patient's anemia and do not address the issues related to excess serum levels of iron. Red blood cell transfusions can treat a patient's anemia but exacerbate the patient's iron overload and are burdensome. The iron overload caused by transfusions will often be treated with chelating agents. However, these agents work very slowly and have significant kidney and liver toxicity issues.

We believe that PTG-300 may be able to restore iron homeostasis to the bone marrow as well as reduce excess circulating iron. We anticipate that restoration of iron homeostasis in the bone marrow – and the resulting increase in red blood cell production – will result in the correction or amelioration anemia as measured by hemoglobin levels. In addition, may beta-thalassemia patients require regular transfusions to treat their anemia. For these patients, treatment with PTG-300 may reduce or eliminate the need for transfusions and related chelation treatments.

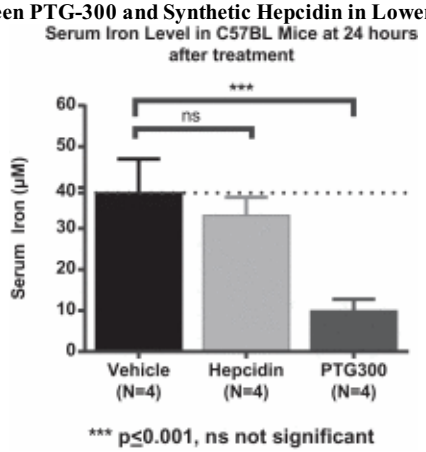
Beta-thalassemia is most prevalent in people of Mediterranean descent, such as Italians, Greeks and Turks, and is also found in people from the Arabian Peninsula, Iran, Africa, Southeast Asia and southern China. Globally, the prevalence of beta-thalassemia was estimated to be approximately 300,000 patients in 2008 according to the Centers for Disease Control. The disease is rarer in the United States where Decision Resources Group ("DRG") estimates there are approximately 3,000 patients. In the major markets of the United States, Italy, Germany, UK, Spain, and France, DRG estimates there are approximately 16,000 diagnosed patients. Most patients with beta-thalassemia suffer from anemia

caused by hepcidin deficiency and a significant number are dependent on transfusions and chelating agents, which can cost between $50,000 to $70,000 per year in the United States.

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

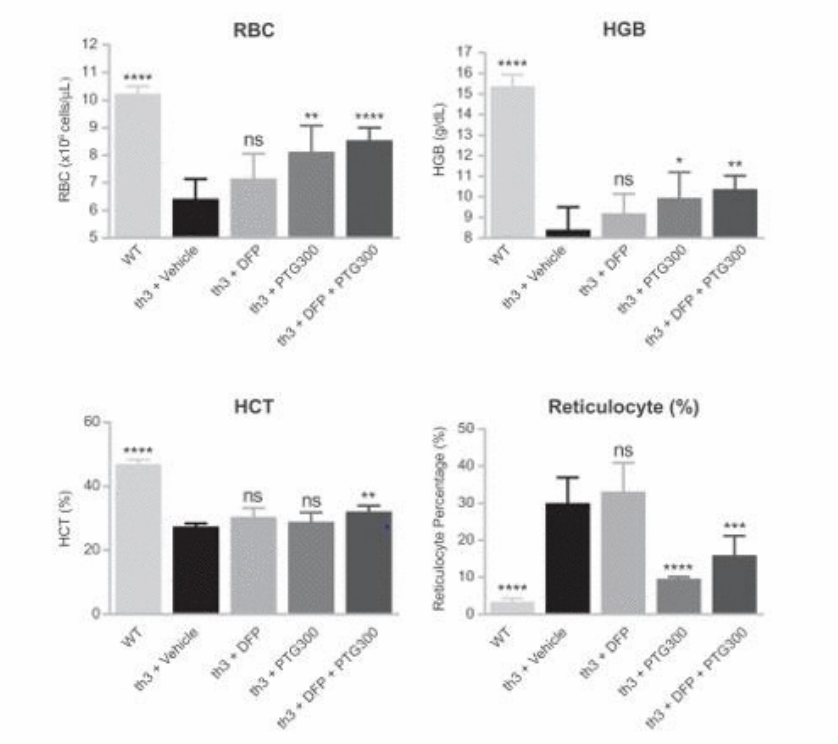
In pre-clinical studies, we demonstrated that PTG-300 can lower serum iron more effectively than hepcidin and maintain such lowered serum iron levels for at least 24 hours following a single subcutaneous injection (Figure 4). We have also demonstrated that PTG-300 in a dose dependent manner can reduce serum iron in healthy mice, rats, and cyno.

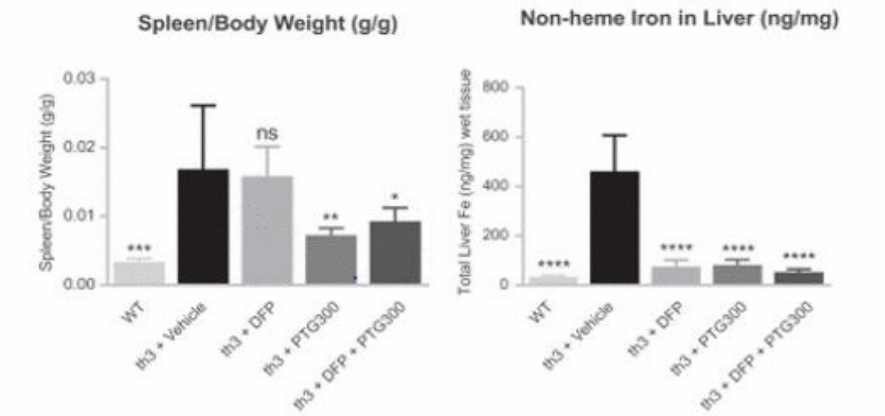
Figure 4: Significant Difference Between PTG-300 and Synthetic Hepcidin in Lowering Serum Iron in Healthy Mice



PTG-300 was also able to address the underlying anemia present in a mouse genetic model of beta-thalassemia, as shown most prominently by the significant increase in red blood cell number (RBC) and hemoglobin (HGB) with the corresponding decrease in reticulocyte content (Figure 5). As a consequence we also observed a significant reduction in the pathological increases in spleen weight (splenomegaly) by addressing the underlying ineffective erythropoiesis. Furthermore, PTG-300 was effective in reducing the increase in liver iron content. In contrast the oral iron chelator deferiprone (DFP) did not correct the anemia or the splenomegaly.

Figure 5: PTG-300 Addresses Ineffective Erythropoiesis in Mouse Beta-thalassemia





DFP dosed at 1.25mg/mL drinking water
1 mg/kg Q2D for 6 weeks (Hbbth3+ Mice)
Statistical significance was assessed by One-way ANOVA with post-hoc Dunnett's method versus Vehicle control: *p≤0.05; **p≤0.01; ***p≤0.001; ****p≤0.0001; ns, not significant.

PTG-300's Phase 1 Clinical Trial Overview

We completed IND-enabling studies during the first half of 2017 and completed a Phase 1 clinical trial during the fourth quarter of 2017. The Phase 1 randomized, placebo-controlled single ascending- and repeat-dose study was conducted to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of PTG-300 in 62 normal healthy male volunteers.

The Phase 1 study demonstrated that PTG-300 induces dose-related reductions in serum iron, which persist beyond 72 hours at higher dose levels. These results were consistent with known activities of hepcidin and pre-clinical studies of PTG-300. In the study, PTG-300 produced dose-dependent increases in blood exposure, and was well tolerated, with no serious adverse events or dose-limiting toxicities. The most common adverse event was a transient and self-limited erythema (redness) at the injection site in some subjects which was largely dose-related. The study provided a pharmacodynamic proof of concept and established a range of doses that could be evaluated in the treatment of beta-thalassemia.

PTG-300's Development Program

In 2018, we anticipate filing an IND as well as ex-U.S. clinical trial applications and initiating a Phase 2 study of PTG-300 in patients with beta-thalassemia. In addition to the potential treatment of anemia in rare blood disorders, such as beta-thalassemia and myelodysplastic syndromes, PTG-300 therapy may also have potential benefit in other diseases such as hereditary hemochromatosis, polycythemia vera, siderophilic infections, and liver fibrosis and we are evaluating potential development pathways for those indications. PTG-300 has received orphan drug designation for the treatment of beta-thalassemia from the FDA.

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 clinical-stage product candidates PTG-100, 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.

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 publicly 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.

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 for 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

Janssen License and Collaboration Agreement

In May 2017, we and Janssen entered into an exclusive license and collaboration agreement (the "Janssen License and Collaboration Agreement") for the development, manufacture and commercialization of PTG-200 worldwide for the treatment of CD and UC. The Janssen License and Collaboration Agreement became effective on July 13, 2017. Upon the effectiveness of the agreement, we received a non-refundable, upfront cash payment of $50.0 million from Janssen. See "Item 7. Management's Discussion and Analysis – Overview" and Note 3 to the Consolidated Financial Statements included elsewhere in this Annual Report on Form 10-K for additional information.

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. See "Item 7. Management's Discussion and Analysis – Contractual Obligations and Other Commitments" and Note 6 to the Consolidated Financial Statements included elsewhere in this Annual Report on Form 10-K for additional information.

Competition

The biotechnology and pharmaceutical industries are intensely competitive and subject to rapid and significant technological change. 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 α4β7 integrins and IL-23 based product candidates for IBD.

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 a4ß7 antibody: Takeda Pharmaceutical Company
- Infused IL-23 and IL-12 antibody: Johnson & Johnson
- Injectable or infused anti-TNFα therapy: AbbVie, Johnson & Johnson, Amgen, Pfizer, UCB S.A., Boehringer Ingelheim, Merck

We are also aware of several companies developing therapeutic product candidates for the treatment of IBD, including, but not limited to AbbVie, Allergan, Atlantic Healthcare Plc, Aprogen (biosimilar TNF-α antibody in Phase 3) Arena Pharmaceuticals, Inc., AstraZeneca, Biogen, Boehringer Ingelheim (adalimumab biosimilar in Pre-Registration), Bristol-Myers Squibb, Celgene (mongersen sodium and ozanimod hydrochloride in Phase 3 clinical trials), Eli Lilly and Company, Galapagos/Gilead (filgotinib in Phase 3), Lycera Corp., Mitsubishi Tanabe Pharma Corporation, Pfizer (tofacitinib citrate in Pre-Registration), Roche/Genentech (etrolizumab in Phase 3), Samsung Bioepis (adalimumab biosimilar in Pre-Registration), Sandoz (adalimumab biosimilar in Phase 3), Shire/Pfizer (PF-00547659), and UCB S.A.

We believe our principal competition in the treatment of chronic iron overload disorders, such as beta-thalassemia and MDS will come from products being developed by companies such as Acceleron (luspatercept in Phase 3), bluebird bio (LentiGlobin in Phase 3), Bristol-Myers Squibb, Emmaus Medical (glutamine in pre-registration), Gilead, Global Blood Therapeutics, Inc., La Jolla Pharmaceutical and Novartis AG, among others. We believe competition will also include approved iron chelation therapies that have been developed by Novartis AG 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 “Item 1A Risk Factors—Risks Related to Our Intellectual Property.”

We have six issued patents and numerous patent applications related to our clinical-stage 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 February 15, 2018, our patent portfolio includes the following:

- four issued patents and more than 50 patent applications that we exclusively own related to α4β7 integrin peptide antagonists;
- one issued patent and more than 50 patent applications that we exclusively own related to IL-23R antagonist peptides;
- one issued patent and approximately 25 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 four issued U.S. patents and more than 50 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 one issued U.S. patent and more than 50 pending 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 April 2038 (worldwide, excluding possible patent term extensions).

Hepcidin Mimetics Analogues

The hepcidin peptide analogues patent portfolio includes one issued U.S. patent and approximately 25 pending 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 February 2039 (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 "Item 1A 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 and quality control 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 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 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 ethics committee ("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 Biologics License Application ("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 program user fee requirements for any marketed products, as well as 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, as well as efforts by the current administration to repeal or replace certain aspects of the ACA. For example, since January 2017, the President has signed two Executive Orders and other directives designed to delay, circumvent, or loosen certain requirements mandated by the ACA. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the ACA. While Congress has not passed comprehensive repeal legislation, two bills affecting the implementation of certain taxes under the ACA were signed into law. The Tax Cuts and Jobs Act of 2017 (the “Tax Act”) includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the “individual mandate”. Additionally, on January 22, 2018, the President signed a continuing resolution

on appropriations for fiscal year 2018 that delayed the implementation of certain ACA-mandated fees, including the so-called "Cadillac" tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. Further , the Bipartisan Budget Act of 2018, or the BBA, among other things, amends the ACA, effective January 1, 2019, to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole", and increase from 50% to 70% the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in the Medicare Part D program. 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 subsequent legislation, including the BBA, will stay in effect through 2027 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.

Further, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products. Such scrutiny has resulted in several recent Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. At the federal level, the current administration's budget proposal for fiscal year 2019 contains further drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. While any proposed measures will require authorization through additional legislation to become effective, Congress and the current administration have both stated that they will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures have become increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

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 ("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; the 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, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, 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 conducted Phase 1 trials for PTG-100 and PTG-300 and are conducting a Phase 1 trial for PTG-200, 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 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 Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use ("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.

Employees

As of December 31, 2017, we had 55 full-time employees, 44 of whom were in research and development, of which 4 hold an M.D. and 14 hold Ph.D. degrees. The remaining 11 employees worked in finance, business development, human resources and administrative support, of which 2 hold a Ph.D. None of our employees are represented by a labor union or covered by a collective bargaining agreement. We consider our relationship with our employees to be good.

Corporate and Other Information

Protagonist Pty Limited ("Protagonist Australia") was incorporated in Australia in September 2001. We were incorporated as a Delaware corporation in 2006, under the name Protagonist Therapeutics, Inc., and became the parent of Protagonist Australia pursuant to a transaction in which all of the issued and outstanding capital stock of Protagonist Australia was exchanged for shares of our common stock and Series A preferred stock. Our principal executive offices are located at 7707 Gateway Boulevard, Suite 140, Newark, California 94560. Our telephone number is (510) 474-0170. Our website address is www.protagonist-inc.com. References to our website address do not constitute incorporation by reference of the information contained on the website, and the information contained on the website is not part of this document.

We make available, free of charge on our corporate website, copies of our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, Proxy Statements, and all amendments to these reports, as soon as reasonably practicable after such material is electronically filed with or furnished to the Securities and Exchange Commission pursuant to Section 13(a) or 15(d) of the Securities Exchange Act. We also show detail about stock trading by corporate insiders by providing access to SEC Forms 3, 4 and 5. This information may also be obtained from the SEC's on-line database, which is located at www.sec.gov. Our common stock is traded on the Nasdaq Stock Market under the symbol "PTGX."

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012. As such, we are eligible for exemptions from various reporting requirements applicable to other public companies that are not emerging growth companies, including, but not limited to, not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act of 2002 and reduced disclosure obligations regarding executive compensation. We will remain an emerging growth company until the earlier of (1) December 31, 2021, (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).

Item 1A. Risk Factors

We have identified the following risks and uncertainties that may have a material adverse effect on our business, financial condition or results of operations. Investors should carefully consider the risks described below before making an investment decision. Our business faces significant risks and the risks described below may not be the only risks we face. Additional risks not presently known to us or that we currently believe are immaterial may also significantly impair our business operations. If any of these risks occur, our business, results of operations or financial condition could suffer, the market price of our common stock could decline and you could lose all or part of your investment in our common stock.

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. Our net loss for the years ended December 31, 2017 and 2016 was approximately $37.0 million and $37.2 million, respectively. As of December 31, 2017, we had an accumulated deficit of $101.6 million. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' equity and working capital. We expect to continue to incur significant research, development and other expenses related to our ongoing operations and product development, including clinical development activities under our exclusive license and collaboration agreement (the "Janssen License and Collaboration Agreement") with Janssen Biotech, Inc., a Pennsylvania corporation ("Janssen"), and as a result, we expect to continue to incur losses in the future 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. Furthermore, any revenues generated from the Janssen License and Collaboration Agreement may not be sufficient alone to sustain our operations as there can be no assurance that we will receive any opt-in election fees, development, regulatory, or sales milestone payments, or royalties from Janssen in the future pursuant to the Janssen License and Collaboration Agreement. 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. 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, PTG-100, PTG-200 and PTG-300, and conducting research to identify additional product candidates. We successfully filed Clinical Trial Notifications in Australia to support our completed Phase 1 clinical trials of PTG-100 and PTG-300 and our ongoing Phase 1 clinical trial of PTG-200. We successfully filed a U.S. IND application, and regulatory submissions in other countries as well, to support our ongoing global Phase 2b study of PTG-100 in ulcerative colitis ("UC"). 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, including payments, if any, under the Janssen License and Collaboration Agreement;
- 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;
- the ability of third party manufacturers to manufacture in accordance with current good manufacturing practices ("cGMP") 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 clinical-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 and PTG-300 in healthy volunteers, we have initiated a global Phase 2b clinical trial of PTG-100 in patients with moderate-to-severe UC and we have initiated a Phase 1 clinical study of PTG-200. 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, PTG-300 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.

Further, in the event our Janssen License and Collaboration Agreement is terminated, we may not receive any development fees, milestone payments, or royalties under the Janssen License and Collaboration Agreement, and we would be required to fund all clinical development, manufacturing, and commercial activities for PTG-200, which would require us to raise additional capital or establish alternative collaborations with third-party collaboration partners, which may not be possible.

As of December 31, 2017, we had cash, cash equivalents and available-for-sale securities of $155.5 million. Based upon our current operating plan and expected expenditures, we believe that our existing cash, cash equivalents, and available-for-sale securities will be sufficient to fund our operations for at least the next 12 months. Our existing capital resources 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 currently expect;
- the achievement of development, regulatory, and sales milestones resulting in the payment to us from Janssen under the Janssen License and Collaboration Agreement and the timing of receipt of such payments, if any;
- changes or delays in our and/or Janssen's development plans for PTG-200;
- the costs of preparing to manufacture PTG-100, PTG-200 or PTG-300 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, PTG-300 or any future product candidate is approved, including the formation of a sales force;
- Janssen's ability to successfully market and sell PTG-200, upon regulatory approval and clearance, in the United States and other countries;
- the timing, receipt and amount of royalties under the Janssen License and Collaboration Agreement on worldwide net sales of PTG-200, upon regulatory approval and clearance, if any;
- the sales price and availability of adequate third-party reimbursement for our product candidates that may receive regulatory approval, if any;
- 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 our existing capital resources, future interest income, upfront payment and potential opt-in election fees, milestone payments, and royalties under the Janssen License and Collaboration Agreement are insufficient to meet future capital requirements, and 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 securities, including any sale of up to $50.0 million worth of shares of our common stock pursuant to our Sales Agreement with Cantor Fitzgerald & Co. (the "Sales Agreement"), 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, PTG-200 and PTG-300, which are in early-stage clinical development, 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 PTG-300 which targets anemia associated with certain rare blood disorders, and the development of other product candidates. 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 and have initiated a global Phase 2b clinical trial of PTG-100 in patients with moderate to severe UC. We also completed a Phase 1 clinical trial for PTG-300 in December 2017 and initiated a Phase 1 clinical trial of PTG-200 in November 2017. We will need to conduct larger, more extensive clinical trials in the target patient populations 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 may 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 are 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 or other regulatory authorities may require post-marketing studies 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; and
- the FDA or comparable foreign regulatory authorities may change their approval policies or adopt new regulations.

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, PTG-200 or PTG-300 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.

If Janssen does not elect to continue the development of PTG-200 through an Opt-In Election, our business and business prospects would be significantly harmed.

Under the terms of the Janssen Collaboration and License Agreement, Janssen is not obligated to make any additional payments to us as we have already received the upfront payment that was due in the third quarter of 2017 pursuant to the terms of the Janssen License and Collaboration Agreement, until such time as it affirmatively elects to continue to advance the development of PTG-200 (the "First Opt-In Election") within a period of time following completion date of the Phase 1 studies and the Phase 2a portion of the CD Phase 2 clinical trial and any related activities set forth in a clinical development plan ("Phase 2a Activities"). The timing of Janssen's First Opt-In Election and whether Janssen elects to continue further clinical development of PTG-200 also affects the timing and availability of potential future milestone and royalty payments, if any. If the Phase 1 clinical trial or Phase 2 activities are terminated early, suspended for an extended period of time, or are otherwise unsuccessful, Janssen may determine not to elect to continue further clinical development of PTG-200, in which case, the Janssen License and Collaboration Agreement would terminate and our business and business prospects would be materially adversely affected.

There may be disagreements between Janssen and Protagonist during the term of the Janssen License and Collaboration Agreement, and if they are not settled amicably or in the favor of Protagonist, the result may harm our business.

We are subject to the risk of possible disagreements with Janssen, including those regarding the development, manufacture, and commercialization of PTG-200, interpretation of the Janssen License and Collaboration Agreement, and ownership of proprietary rights. In addition, in certain circumstances, we may believe that a particular milestone has been achieved and Janssen may disagree with our belief. In that case, receipt of that milestone payment may be delayed or may never be received, which would adversely affect our financial condition and may require us to adjust our operating plans.

The joint governance structure contemplated by the Janssen License and Collaboration Agreement will cease to have decision-making authority once the development term ends, which will preclude our ability to participate in any further decision-making for PTG-200. Reliance on a joint governance structure also subjects us to the risk that changes in key management personnel who are members of the various joint committees may materially and adversely affect the functioning of these committees, which could significantly delay or preclude PTG-200 development and/or commercialization. As a result of possible disagreements with Janssen, we also may become involved in litigation or arbitration, which would be time-consuming for our management and employees and expensive.

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 is in an ongoing global Phase 2b trial, PTG-300, which completed a Phase 1 clinical trial in December 2017, and PTG-200, which is in a Phase 1 clinical trial. 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, 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, PTG-200 and PTG-300, our lead product candidates, or any other product candidate, 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 our 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 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 if we complete such filings. 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 only recently initiated a Phase 2 clinical trial and have never conducted a Phase 3 clinical trial or submitted an 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, well-controlled clinical 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 only recently initiated a Phase 2 clinical trial and have never conducted a Phase 3 clinical trial or submitted an 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 the current Phase 2 clinical trial 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 CROs, 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 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. There are a significant number of global clinical trials in ulcerative colitis that are currently ongoing, especially in Phases 2 and 3, making it highly competitive and challenging to recruit subjects. 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, PTG-200 and PTG-300 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, PTG-200, and PTG-300. 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 for PTG-100 and PTG 200, we seek to develop peptide-based product candidates against validated biological targets and pathways that have been targeted 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 α4ß7 integrin antagonist that targets the same target as the currently marketed injectable antibody drug, Entyvio®, approved for treatment in UC and CD, and PTG-200 targets the IL-23 biological pathway, which is a pathway targeted by the currently marketed injectable antibody drug, Stelara®, approved for treatment of psoriasis, psoriatic arthritis, and CD. 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 unsuccessful or 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.

If there are any safety or efficacy results that cause the benefit-risk profile of PTG-200 to become unacceptable, the clinical development of PTG-200 would be delayed or halted, and as a result, Janssen may terminate the Janssen License and Collaboration Agreement, which would severely and adversely affect our business prospects, and may cause us to cease operations.

PTG-200 may prove to have undesirable or unintended side effects or other characteristics adversely affecting its safety, efficacy or cost effectiveness that could prevent or limit its approval for marketing and successful commercial use, or that could delay or prevent the commencement and/or completion of clinical trials for PTG-200. If regulatory submissions requesting approval to market PTG-200 are submitted, after reviewing the data in such submissions, the FDA and regulatory agencies in other countries may conclude that the overall benefit-risk profile of PTG-200 treatment is unacceptable, and the clinical development of PTG-200 would be delayed or halted. Any of these events would severely harm our business and prospects.

Clinical trials by their nature examine the effects of a potential therapy in a sample of the potential future patient population. As such, clinical trials conducted with PTG-200 may not uncover all possible adverse events that patients treated with PTG-200 may experience. In collaboration with Janssen, we may in the future observe or report dose-limiting or other safety issues in potential future clinical trials of PTG-200. If such toxicities or other safety issues in any clinical trial of PTG-200 result in an unacceptable benefit-risk profile, then:

- the commencement and/or completion of any future clinical trials would likely be delayed or prevented; or
- additional, unforeseen trials, or preclinical studies may be required to be conducted.

The occurrence of any of these events may cause Janssen to abandon their development of PTG-200 entirely and terminate the Janssen License and Collaboration Agreement. Any termination of the Janssen License and Collaboration Agreement by Janssen would have a material adverse effect on our results of operations, financial condition, business prospects and the future of PTG-200.

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 United States, 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 face a variety of manufacturing risks and rely 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 current good manufacturing practices and for Europe and other major countries, International Council for 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 particular, as we proceed with the development and potential commercialization of PTG-100, we will need to increase the scale at which the drug is manufactured which will require the development of new manufacturing processes to potentially reduce the cost of goods. We will rely on our internal process research and development efforts and those of contract manufacturers to develop the GMP manufacturing processes required for cost-effective and large scale production. If these efforts are not successful in developing cost-effective processes and if the contract manufacturers are not successful in converting it to commercial scale manufacturing, then our development and/or commercialization of PTG-100 could be materially adversely affected. 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.

In March 2018, we were granted orphan drug designation in the United States by the FDA for PTG-300 for the treatment of patients with beta-thalassemia. Despite this designation, we may be unable to maintain the benefits associated with orphan drug designation status, including market exclusivity. If PTG-100 or PTG-200 is developed for the treatment of pouchitis, pediatric IBD or an alternate orphan indication, we may file for orphan drug designation with respect to such indication. We may not be the first to obtain regulatory approval of a product candidate for the beta-thalassemia or any other orphan-designated indication that we may pursue 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.

Other than our Janssen License and Collaboration Agreement, we have no current collaborations for any of our product candidates. Even if we are able to establish other collaboration arrangements, any such collaboration, including the Janssen License and Collaboration Agreement, 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.

We believe our principal competition in the treatment of IBD is from companies with approved agents in the following therapeutic classes, among others:

- Infused α4ß7 antibody: Takeda Pharmaceutical Company
- Infused IL-23 and IL-12 antibody: Johnson & Johnson
- Injectable or infused anti-TNFα therapy: AbbVie, Johnson & Johnson, Amgen, Pfizer, UCB S.A., Boehringer Ingelheim, Merck

We are also aware of several companies developing therapeutic product candidates for the treatment of IBD, including, but not limited to AbbVie, Allergan, Atlantic Healthcare Plc, Aprogen (biosimilar TNF-α antibody in Phase 3) Arena Pharmaceuticals, Inc., AstraZeneca, Biogen, Boehringer Ingelheim (adalimumab biosimilar in Pre-Registration), Bristol-Myers Squibb, Celgene (mongersen sodium and ozanimod hydrochloride in Phase 3 clinical trials), Eli Lilly and Company, Galapagos/Gilead (filgotinib in Phase 3), Lycera Corp., Mitsubishi Tanabe Pharma Corporation, Pfizer (tofacitinib citrate in Pre-Registration), Roche/Genentech (etrolizumab in Phase 3), Samsung Bioepis (adalimumab biosimilar in Pre-Registration), Sandoz (adalimumab biosimilar in Phase 3), Shire/Pfizer (PF-00547659), and UCB S.A.

We believe our principal competition in the treatment of chronic iron overload disorders, such as beta-thalassemia, myelodysplastic syndromes will come from other pipeline products being developed by companies such as Acceleron (luspatercept in Phase 3), bluebird bio (LentiGlobin in Phase 3), Bristol-Myers Squibb, Emmaus Medical (glutamine in pre-registration), Gilead, Global Blood Therapeutics, Inc., La Jolla Pharmaceutical and Novartis AG, among others. We believe competition will also include approved iron chelation therapies that have been developed by Novartis AG 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 have not yet negotiated our agreement with Janssen specifying all of the terms of our Co-Detailing Option and would need to develop our own internal sales force.

Pursuant to the Janssen License and Collaboration Agreement, we have a co-detailing option, which, if PTG-200 is approved for commercial sale, allows us to elect to provide up to 30% of the PTG-200 selling effort in the United States with sales force personnel (the "Co-Detailing Option"). While the Janssen License and Collaboration Agreement includes the material terms of our Co-Detailing Option, Janssen and we mutually agreed to negotiate a separate agreement specifying the detailed activities and responsibilities in respect of the marketing and co-promotion of PTG-200 following our election to exercise our Co-Detailing Option. We will need to negotiate this separate agreement with Janssen and, as a result, Janssen may place restrictions or additional obligations on us, including financial obligations. Any restrictions or additional obligations may restrict our co-detailing activities or involve more significant financial or other obligations than we currently anticipate. In addition, we have no sales experience as a company. There are risks involved with establishing our own sales force capabilities. Developing an internal sales force and function will require substantial expenditures and will be time-consuming, may expose us to unforeseen costs and expenses, and we may not be able to effectively recruit, train or retain sales personnel. Accordingly, we may be unable to establish our own sales force which could effectively preclude our ability to take any advantage of participating in co-detailing PTG-200 in the United States. In addition, any sales force we establish may not be effective, or may be less effective than the any sales force that Janssen utilizes to promote PTG-200. In such event, the commercialization of PTG-200 may be adversely affected, which could materially and adversely affect any sales milestone payments or royalties we may receive under the Janssen License and Collaboration Agreement.

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, and in the case of the Janssen License and Collaboration Agreement, we may elect to exercise our Co-Detailing Option, which would require us to establish a U.S. sales team. 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 PTG-100 and PTG-200, GI-restricted drugs that target the same biological pathways as currently marketed injectable antibody drugs for the treatment of IBD and the development of PTG-300 for treatment of anemia associated with certain rare blood disorders. 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 or 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 program 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 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 or 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 and their implementing regulations, which also imposes obligations, including mandatory contractual terms, on HIPAA-covered entities and their business associates 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 Payments 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; 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, integrity oversight and reporting obligations, 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, and to the extent that, Janssen or we are unable to comply with these regulations, our ability to earn potential royalties from worldwide net sales of PTG-200 would be materially and adversely impacted. 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. The imposition of any of these penalties or other commercial limitations could negatively impact our collaboration with Janssen or cause Janssen to terminate the Janssen License and Collaboration Agreement, either of which would materially and adversely affect our business, financial condition and results of operations.

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% (70% commencing January 1, 2019) 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.

Some of the provisions of the ACA have yet to be implemented, and there have been judicial and Congressional challenges to certain aspects of the ACA, as well as recent efforts by the current administration to repeal or replace certain aspects of the ACA. Since January 2017, the President has signed two Executive Orders and other directives designed to delay the implementation of any certain provisions of the ACA or otherwise circumvent some of the requirements for health insurance mandated by the ACA. Concurrently, Congress has considered legislation that would repeal or repeal and replace all or part of the ACA. While Congress has not passed comprehensive repeal legislation, two bills affecting the implementation of certain taxes under the ACA have been enacted. The Tax Cuts and Jobs Act of 2017 (the "Tax Act") includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." Additionally, on January 22, 2018, the President signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain fees mandated fees under the ACA, including the so-called "Cadillac" tax on certain high cost employer-sponsored insurance plans, the

annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. Congress may consider other legislation to repeal or replace other elements of the ACA

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, including the BBA, will remain in effect through 2027 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.

Further, there has been heightened governmental scrutiny over the manner in which manufacturers set prices for their marketed products. Such scrutiny has resulted in several recent Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. At the federal level, the current administration's budget proposal for fiscal year 2019 contains further drug price control measures that could be enacted during the 2019 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. While any proposed measures will require authorization through additional legislation to become effective, Congress and the current administration have both stated that they will continue to seek new legislative and/or administrative measures to control drug costs. At the state level, legislatures have become increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

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, and Tom O'Neil, our Chief Financial Officer. 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, our collaboration 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 December 31, 2017, we had 55 full-time employees, including 44 employees engaged in research and development. 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, collaboration partner, and other third parties on which we rely may 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, cyber, auto liability, workers' compensation, clinical trial, 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 to insure risks which could arise from our operations. Any significant uninsured losses or liabilities may require us to pay substantial amounts from corporate cash intended to fund operations, 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.

If we, or our contractors or agents are unable to comply with federal, state and county environmental and safety laws and regulations, including those governing laboratory procedures and the handling of biohazardous materials,

chemicals and various radioactive compounds, considerable additional costs or liabilities could be assessed that would have a material adverse effect on our financial condition. We, our collaborators, contractors or agents may be required to incur significant costs to comply with current or future environmental laws and regulations and may be adversely affected by the cost of compliance with these laws and regulations.

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 clinical trial liability insurance 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 than 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. 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 or other challenge 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 (the "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 issued patents 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 patents 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 or derivation proceedings provoked by third parties or brought by us, the PTO or any foreign patent authority may be necessary to determine the priority or ownership 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, interference or derivation 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 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 United States, 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 parties 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 of 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.

As more groups become engaged in scientific research and product development in fields related to our product candidates, such as the IL-23 receptor, the risk of our patents, or patents that we have in-licensed, being challenged through patent interferences, derivation proceedings, oppositions, re-examinations, litigation or other means will likely increase. Challenges to our patents through these procedures can be extremely expensive and time-consuming, even if the outcome is favorable to us. An adverse outcome in a patent dispute could have a material adverse effect on our business by:

- causing us to lose patent rights in the relevant jurisdiction(s);
- subjecting us to litigation, or otherwise preventing Janssen or us from commercializing PTG-200 or other product candidates in the relevant jurisdiction(s);
- requiring Janssen or us to obtain licenses to the disputed patents;
- forcing Janssen or us to cease using the disputed technology; or
- requiring Janssen or us to develop or obtain alternative technologies.

An adverse outcome in a patent dispute could severely harm our collaboration with Janssen or cause Janssen to terminate the Janssen License and Collaboration Agreement. Additionally, if patent protection is not available on any patents we have licensed to Janssen in one or more countries, our potential royalties obtained in those countries from Janssen may be non-existent or lower than we currently expect and could be reduced in accordance to the terms of the Janssen License and Collaboration Agreement.

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. For example, our granted U.S. patents covering PTG-100 and PTG-200 expire in 2035, and our granted U.S. patent covering PTG-300 expires in 2034. 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 ("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.

On September 26, 2017, Medical Diagnostic Laboratories, LLC ("MDL") filed a lawsuit for alleged infringement of U.S. Patent No. 8,946,150 ("the '150 patent") by Protagonist's polypeptide PTG-200 (the "Complaint"). We have licensed PTG-200 to Janssen Biotech, Inc. for clinical development. On December 1, 2017, we filed a motion to dismiss the case, urging that all of our activities, as described in the Complaint, fall within the safe harbor of 35 U.S.C. 271(e)(1) – precluding infringement for FDA-research related activities. On February 7, 2018, our motion to dismiss the case was granted by the U.S. District Court for the Northern District of California. This case is described in further detail below in Item 3. "Legal Proceedings". If further actions occur and we fail in defending any such claims, in addition to paying monetary damages, we may be enjoined from marketing PTG-200 and other IL-23 inhibitor compounds. 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.

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 patents, 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-U.S. 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 are prosecuted and may also affect patent litigation. The PTO has developed regulations and procedures to govern administration of the Leahy-Smith Act, but 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 patents or any pending patent applications we may have;
- we might not have been the first to make the inventions covered by the issued patents or pending patent applications 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 patents 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 patents, 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 patents, 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.

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 Ownership of our Common Stock

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 has been, and 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 Annual Report on Form 10-K, 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.

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 and will be able to exert significant control over matters subject to stockholder approval.

Our executive officers, directors, holders of 5% or more of our capital stock and their respective together beneficially own a significant percentage of our stock. Therefore, 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 material weaknesses 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 the IPO, 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, 2015 and 2014, 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, 2015 and 2014. 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 accordance with Section 404 of the Sarbanes-Oxley Act. We have taken steps to remediate the material weaknesses, including increasing the depth and experience within our accounting and finance organization, and implemented an approval process related to manual journal entries and the related supporting journal entry calculations. In addition, we continued to work on designing and implementing additional improved processes and internal controls. We have completed the implementation of this plan as of December 31, 2017, and management determined that we have remediated the material weaknesses as of December 31, 2017. We can give no assurance 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 controls over financial reporting could result in errors in our financial statements that could result in a restatement of our financial statements and cause us to fail to meet our reporting obligations.

We are 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 common stock.

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 year ended December 31, 2017.

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 have begun 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 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 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 the IPO, (b) in which we have total annual gross revenue of at least $1.07 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."

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, 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. At December 31, 2017, we had outstanding a total of 21,088,306 shares of common stock, notwithstanding any potential exercises of outstanding options and issuance of shares under the employee stock purchase plan.

If 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.

Any sales of securities by our stockholders could 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, including any sale of up to $50.0 million worth of shares of our common stock pursuant to our sales agreement with Cantor Fitzgerald & Co. (the "Sales Agreement"). our Sales Agreement, if we need to raise additional capital. The number of shares 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, including any sale of up to $50.0 million worth of shares of our common stock pursuant to the Sales Agreement, our common stockholders would experience additional dilution and, as a result, our stock price may decline.

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

We have incurred and will continue to 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 have devoted and will continue to need to devote a substantial amount of time to ensure that we comply with all of these requirements. 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.

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.

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, since we have material weaknesses 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.

Any changes to existing accounting pronouncements or taxation rules or practices may cause adverse fluctuations in our reported results of operations or affect how we conduct our business.

A change in accounting pronouncements or taxation rules or practices can have a significant effect on our reported results and may affect our reporting of transactions completed before the change is effective. New accounting pronouncements, taxation rules and varying interpretations of accounting pronouncements or taxation rules have occurred in the past and may occur in the future. The change to existing rules, future changes, if any, or the need for us to modify a current tax or accounting position may adversely affect our reported financial results or the way we conduct 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.

Our common stock is listed on The Nasdaq Global Market. 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 by the research and reports that securities or industry analysts publish about us or our business. In the event 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 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.

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.

Our amended and restated certificate of incorporation provides that the Court of Chancery of the State of Delaware is 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 provides 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 acquirer from conducting a solicitation of proxies to elect the acquirer'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.

The recently passed comprehensive tax reform bill could adversely affect our business and financial condition.

On December 22, 2017, new tax legislation (the "Tax Act") was enacted which significantly changes the Internal Revenue Code, as amended (the "Code"). The Tax Act, among other things, contains significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%; limitation of the tax deduction for interest expense to 30% of adjusted earnings; for net operating losses generated after 2017, limitation of the deduction to 80% of current year taxable income, indefinite carryforward of net operating losses and elimination of net operating loss carrybacks; changes in the treatment of offshore earnings regardless of whether they are repatriated; mandatory capitalization of research and development expenses beginning in 2022; immediate deductions for certain new investments instead of deductions for depreciation expense over time; further deduction limits on executive compensation; and modifying, repealing and creating many other business deductions and credits, including the reduction in the orphan drug credit from 50% to 25% of qualifying expenditures. We continue to examine the impact this tax reform legislation may have on our business. Notwithstanding the reduction in the corporate income tax rate, the overall impact of the Tax Act is uncertain and our business and financial condition could be adversely affected. The impact of this tax reform on holders of our common stock is also uncertain and could be adverse. This annual report does not discuss any such tax legislation or the manner in which it might affect us or our stockholders in the future. We urge our stockholders to consult with their legal and tax advisors with respect to such legislation.

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 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. Based on a review of our equity transactions since inception, we believe a portion of our net operating loss carryforwards and credit carryforwards may be limited due to an equity financing that occurred in 2015. We may experience ownership changes in the future or subsequent shifts in our stock ownership, some of which are outside our control. As of December 31, 2017, we had federal net operating loss carryforwards of approximately $79.2 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.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

We lease approximately 42,877 square feet of office and laboratory space in Newark, California under a lease agreement that expires in May 2024. We believe that our existing facilities 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.

Item 3. Legal Proceedings

We may become subject to litigation and claims arising in the ordinary course of business, including the matter described below.

On September 26, 2017, Medical Diagnostic Laboratories, LLC ("MDL") filed a lawsuit for alleged infringement of U.S. Patent No. 8,946,150 ("the '150 patent") by Protagonist's polypeptide PTG-200 (the "Complaint"). We have licensed PTG-200 to Janssen Biotech, Inc. for clinical development. On December 1, 2017, we filed a motion to dismiss the case, urging that all of our activities, as described in the Complaint, fall within the safe harbor of 35 U.S.C. 271(e)(1) – precluding infringement for FDA-research related activities. On February 7, 2018, our motion to dismiss the case was granted by the U.S. District Court for the Northern District of California. The Court dismissed the case without prejudice to MDL attempting to amend its Complaint within thirty days to attempt to allege new facts that would support a case or suing in the future when commercial activity is imminent or concrete.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities

Market Information

Our common stock began trading on The Nasdaq Global Market on August 11, 2016 and trades under the symbol "PTGX." Prior to such time, there was no public market for our common stock. The following table sets forth the range of high and low quarterly sales prices per share of our common stock for the periods noted, as reported on The Nasdaq Global Market:

	Prices	
	High	Low
2017		
First Quarter	$ 22.50	$ 12.10
Second Quarter	$ 14.85	$ 8.00
Third Quarter	$ 18.37	$ 10.26
Fourth Quarter	$ 21.31	$ 14.10
2016		
Third Quarter (from August 11, 2016)	$ 22.56	$ 10.02
Fourth Quarter	$ 26.36	$ 17.45

On February 28, 2018, the last reported sale price on The Nasdaq Global Market for our common stock was $16.95.

Stockholders

As of the close of business on February 28, 2018, there were 7 stockholders of record of our common stock. The number of stockholders of record is based upon the actual number of stockholders registered at such date and does not include holders of shares in "street names" or persons, partnerships, associates, or corporations, or other entities identified in security listings maintained by depositories.

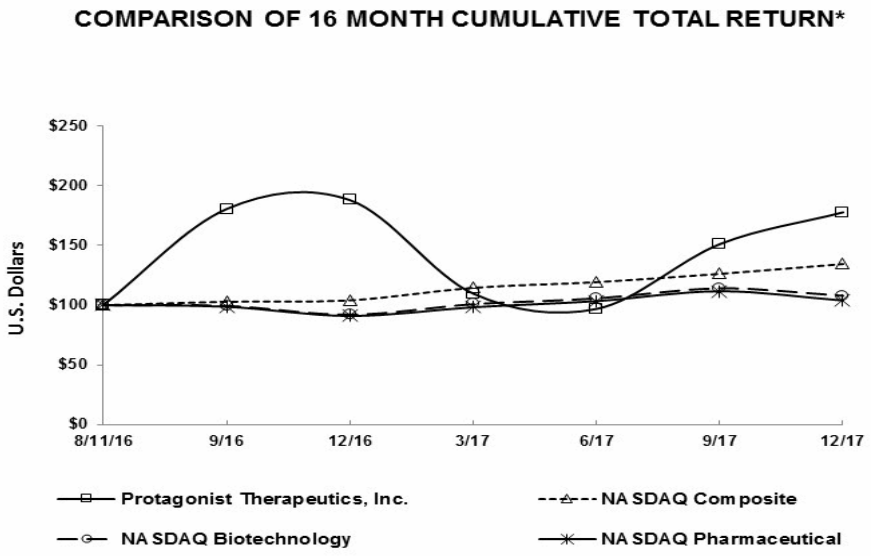
Dividend Policy

We have never declared or paid any cash dividends. We currently expect to retain all future earnings, if any, for use in the operation and expansion of our business, and therefore do not anticipate paying any cash dividends in the foreseeable future.

Performance Graph

The following is not deemed "filed" with the Securities and Exchange Commission and is not to be incorporated by reference into any filing we make under the Securities Act of 1933, as amended, whether made before or after the date hereof and irrespective of any general incorporation by reference language in such filing. The graph below matches shows the cumulative total stockholder return assuming the investment on the date specified in each of our common stock, the Nasdaq Composite Index, the Nasdaq Biotechnology Index, and the Nasdaq Pharmaceutical Index. The graph

tracks the performance of a $100 investment in our common stock and in each index (with the reinvestment of all dividends) from August 11, 2016 to December 31, 2017.



	8/11/2016	9/30/2016	12/31/2016	3/31/2017	6/30/2017	9/30/2017	12/31/2017
Protagonist Therapeutics, Inc.	$ 100.00	$ 180.60	$ 187.95	$ 109.49	$ 96.67	$ 151.03	$ 177.78
Nasdaq Composite	$ 100.00	$ 102.96	$ 104.15	$ 114.76	$ 119.50	$ 126.54	$ 134.81
Nasdaq Biotechnology	$ 100.00	$ 99.61	$ 92.23	$ 101.02	$ 105.80	$ 114.25	$ 108.02
Nasdaq Pharmaceutical	$ 100.00	$ 98.65	$ 91.21	$ 98.28	$ 103.23	$ 111.19	$ 103.69

* *The stock price performance included in this graph is not necessarily indicative of future stock price performance.*

Sale of Unregistered Securities

None.

Repurchases of Shares or of Company Equity Securities

None.

Use of Proceeds from our Public Offering of Common Stock

On August 16, 2016, we closed our initial public offering ("IPO") and issued and sold 7,500,000 shares of our common stock at an initial offering price of $12.00 per share (File Nos. 333-212476 and 333-213071). We received an aggregate of $83.6 million in cash, net of underwriting discounts and commissions, after deducting offering costs. In addition, at the closing of the IPO, all outstanding shares of the redeemable convertible preferred stock converted into

8,577,571 shares of common stock. In September 2016, we issued and sold an additional 252,972 shares of our common stock at a price of $12.00 per share following the underwriters' exercise of their option to purchase additional shares.

Leerink Partners LLC, Barclays Capital Inc. and BMO Capital Markets Corp. acted as the underwriters. Shares of the Company's common stock began trading on the Nasdaq Global Market on August 11, 2016. The shares were registered under the Securities Act on registration statements on Form S-1 (File Nos. 333-212476 and 333-213071). There has been no material change in the planned use of proceeds from the IPO from that described in the prospectus filed with the SEC pursuant to Rule 424(b)(4) under the Securities Act on August 10, 2016.

Item 6. Selected Financial Data

The following selected consolidated statement of operations data for the years ended December 31, 2017, 2016, and 2015 and the consolidated balance sheet data as of December 31, 2017 and 2016 are derived from our audited consolidated financial statements that are included elsewhere in this report. The selected consolidated statement of operations data for the year ended December 31, 2014 and the consolidated balance sheet data at December 31, 2015 and 2014 have been derived from our audited consolidated financial statements which are not included in this report. The data set forth below is not necessarily indicative of results of future operations and should be read in conjunction with "Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations" and "Item 8. Financial Statements and Supplementary Data" included in this Annual Report on Form 10-K to fully understand factors that may affect the comparability of the information presented below:

	Year Ended December 31,			
	2017	2016	2015	2014
	(In thousands, except for share and per share data)			
Consolidated Statement of Operations Data:				
License and collaboration revenue - related party	$ 20,063	$ —	$ —	$ —
Operating expenses:				
Research and development	46,181	25,705	11,831	7,459
General and administrative	11,779	6,961	2,963	1,860
Total operating expenses	57,960	32,666	14,794	9,319
Loss from operations	(37,897)	(32,666)	(14,794)	(9,319)
Interest income	940	242	19	16
Change in fair value of redeemable convertible preferred stock tranche and warrant liabilities	—	(4,719)	(83)	(1,769)
Other expense	—	(34)	—	—
Net loss	$ (36,957)	$ (37,177)	$ (14,858)	$ (11,072)
Net loss attributable to common stockholders	$ (36,957)	$ (37,735)	$ (14,933)	$ (11,218)
Net loss per share attributable to common stockholders, basic and diluted	$ (2.09)	$ (5.80)	$ (59.32)	$ (49.38)
Weighted-average shares used to compute net loss per share attributable to common stockholders, basic and diluted	17,694,505	6,501,796	251,717	227,197

	December 31,			
	2017	2016	2015	2014
	(In thousands)			
Consolidated Balance Sheet Data:				
Cash, cash equivalents and available-for-sale securities	$ 155,459	$ 87,749	$ 11,923	$ 9,324
Working capital	108,392	76,809	11,080	8,563
Total assets	163,734	93,990	14,845	10,328
Deferred revenue - related party	31,752	—	—	—
Redeemable convertible preferred stock tranche liability	—	—	1,643	—
Redeemable convertible preferred stock warrant liability	—	—	480	1,023
Redeemable convertible preferred stock	—	—	36,996	20,576
Accumulated deficit	(101,550)	(64,593)	(27,416)	(12,558)
Total stockholders' equity (deficit)	120,632	87,555	(27,400)	(12,621)

Item 7. 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 "Item 6. Selected Financial Data" and the consolidated financial statements and related notes included elsewhere in this Annual Report. This discussion contains forward-looking statements based upon current expectations that involve risks and uncertainties. Our actual results may differ materially from those anticipated in these forward-looking statements as a result of various factors, including those discussed in "Item 1A. Risk Factors" and in other parts of this Annual Report.

Overview

We are a clinical stage biopharmaceutical company with a proprietary technology platform that enables the discovery and development of novel constrained peptide-based drug candidates that address significant unmet medical needs. Our product candidates are designed to affect critical steps in the biological pathways of particular diseases, for example, by blocking protein-protein interactions. We believe our peptide-based approach has advantages over alternative approaches such as small molecules and antibodies. Two of our clinical stage product candidates, PTG-100 and PTG-200, are potential first-in-class oral drugs that block biological pathways currently targeted by marketed injectable antibody drugs and offer targeted delivery to the gastrointestinal ("GI") tissue compartment. We believe that, as compared to antibody drugs, these product candidates have the potential to provide improved safety due to minimal exposure in the blood, increased convenience and compliance due to oral delivery, and the opportunity for the earlier introduction of targeted therapy. As a result, if approved, they may transform the existing treatment paradigm for inflammatory bowel disease ("IBD"), a GI disease consisting primarily of ulcerative colitis ("UC"), and Crohn's disease ("CD"). Our third clinical stage product candidate, PTG-300, mimics the effect of the hormone hepcidin and has the potential to treat the anemia caused by certain rare blood disorders.

PTG-100, a potential first-in-class oral, alpha-4-beta-7 ("α4β7") integrin antagonist, is currently in a global Phase 2b clinical trial for the treatment of moderate-to-severe UC that is anticipated to randomize approximately 240 patients at approximately 100 clinical sites. We anticipate conducting an interim futility analysis in the first quarter of 2018 and reporting top-line results in the fourth quarter of 2018. If this trial is successful, we anticipate conducting end-of-Phase 2 meetings with global health authorities and initiating pivotal clinical development programs in both UC and CD in 2019. We also anticipate developing PTG-100 for the treatment of chronic pouchitis, a GI condition that occurs in many post-surgical IBD patients. We have completed a pre-Investigational New Drug ("IND") meeting with the FDA regarding the development pathway for PTG-100 in this indication and anticipate proceeding with clinical development activities pending a successful outcome of the Phase 2b futility analysis.

PTG-200 is a potential first-in-class oral Interleukin-23 receptor ("IL-23R") antagonist for the treatment of IBD. It is currently in a Phase 1 healthy volunteer clinical study that was initiated in the fourth quarter of 2017. We have entered into a worldwide license and collaboration agreement with Janssen Biotech, Inc. ("Janssen"), a Johnson and Johnson company, to co-develop and co-detail PTG-200 for all indications, including IBD. See the section below titled "Janssen License and Collaboration Agreement" for additional information.

Our novel peptides have potential applicability in a wide range of therapeutic areas in addition to GI diseases. Our third product candidate, PTG-300, is a mimic of the hormone hepcidin that we are developing for the treatment of anemia in certain rare blood disorders, with an initial focus on beta-thalassemia. In the fourth quarter of 2017, we completed a successful Phase 1 study of PTG-300 in healthy volunteers which established pharmaceutical proof of concept. In 2018, we anticipate filing an IND in the United States and related clinical trial applications outside the United States and initiating a Phase 2 study of PTG-300 in patients with beta-thalassemia. PTG-300 has received an orphan drug designation from the FDA for the treatment of beta-thalassemia.

In addition, we continue to use our peptide technology platform to discover product candidates against targets in disease areas with significant unmet medical needs. In 2018, we anticipate initiating IND-enabling studies for a fourth product candidate, an oral peptide targeting a GI condition other than IBD.

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 and we do not anticipate that we will achieve sustained profitability in the near term. Our net loss was $37.0 million, $37.2 million and $14.8 million for the years ended December 31, 2017, 2016 and 2015, respectively. As of December 31, 2017, we had an accumulated deficit of $101.6 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 continue to incur significant research, development and other expenses related to our ongoing operations and product development, including clinical development activities under the Janssen License and Collaboration Agreement, and as a result, we expect to continue to incur losses in the future as we continue our development of, and seek regulatory approval for, our product candidates.

In August 2016, we completed our initial public offering ("IPO") of our common stock pursuant to which we issued 7,500,000 shares of our common stock at a price of $12.00 per share. In September 2016, we issued an additional 252,972 shares of our common stock at a price of $12.00 per share following the underwriters' exercise of their option to purchase additional shares. We received an aggregate of $83.6 million in cash from the IPO, net of underwriting discounts and commissions, and after deducting offering costs paid by us.

In October 2017, we completed an underwritten public offering of our common stock pursuant to which we issued 3,530,000 shares of our common stock at a public offering price of $17.00 per share. In November 2017, we issued an additional 529,500 shares of our common stock at a price of $17.00 per share following the underwriters' exercise of their option to purchase additional shares. Net proceeds, after deducting underwriting commissions and offering costs, were $64.5 million.

Janssen License and Collaboration Agreement

On May 26, 2017, we and Janssen Biotech, Inc., ("Janssen"), one of the Janssen Pharmaceutical Companies of Johnson & Johnson, entered into an exclusive license and collaboration agreement (the "Janssen License and Collaboration Agreement") for the development, manufacture and commercialization of PTG-200 worldwide for the treatment of CD and UC. Janssen is a related party to us as Johnson & Johnson Innovation - JJDC, Inc., a significant shareholder of ours, and Janssen are both subsidiaries of Johnson and Johnson. The Janssen License and Collaboration Agreement became effective on July 13, 2017. Upon the effectiveness of the agreement, we became eligible for and received a non-refundable, upfront cash payment of $50.0 million from Janssen.

Under the Janssen License and Collaboration Agreement, we granted to Janssen an exclusive worldwide license to develop, manufacture and commercialize PTG-200 and related IL-23R compounds for all indications, including CD and UC. We are responsible, at our own expense, for the conduct of the Phase 1 clinical trial for PTG-200 and Janssen will be responsible for the conduct of a potential Phase 2 clinical trial for PTG-200 in CD, including filing the Phase 2 IND. All such clinical trials will be conducted in accordance with a mutually agreed upon clinical development plan and budget. Development costs for the Phase 2 clinical trial will be shared between the parties on an 80%/20% basis, with Janssen assuming the larger share. Should Janssen elect to retain its license following completion of the Phase 2 clinical trial, it will be responsible, at its own expense, for the manufacture, continued development of, seeking regulatory approval for, and commercialization of PTG-200 worldwide. The parties' development activities under the Janssen License and Collaboration Agreement through the Phase 2 clinical trial will be overseen by a joint governance structure which will have equal representation by both parties unless both parties mutually agree to disband such structure or we have provided written notice to Janssen of our intention to disband and no longer participate in such structure.

We are eligible to receive a $25.0 million payment upon filing of the Phase 2 IND. Following the conclusion of the planned Phase 2a portion of the Phase 2 clinical trial, if Janssen elects to maintain its license rights and continue the development of PTG-200 in the Phase 2b portion of such clinical trial (the "First Opt-in Election"), we would be eligible to receive a $125.0 million payment. Following the conclusion of the planned Phase 2b portion of the Phase 2 clinical trial, if Janssen elects again to maintain its license rights (the "Second Opt-in Election"), we would be eligible to receive a $200.0 million payment. In addition to the opt-in fees, we are eligible to receive additional potential development, regulatory and sales milestone payments of up to an aggregate of $590.0 million, and tiered royalties paid as a percentage of Janssen's worldwide net sales at rates ranging from ten to the mid-teens, with certain customary reductions

under certain circumstances. If Janssen does not make either the First Opt-in Election or the Second Opt-in Election, the Janssen License and Collaboration Agreement will terminate. If Janssen does not make the Second Opt-in Election, or if at any time after the Second Opt-in Election, Janssen terminates the Janssen License and Collaboration Agreement, we would be obligated to pay Janssen a low single-digit royalty on worldwide net sales of PTG-200. We would also have an option to provide up to 30% of the required U.S. details for PTG-200 to prescribers, using our own sales force personnel, upon commercial launch in the United States. If such right is exercised, our detailing costs would be reimbursed by Janssen, at a mutually agreed upon cost per primary detailing equivalent.

The Janssen License and Collaboration Agreement contains customary representations, warranties and covenants by us and Janssen and includes an obligation by us not to develop or commercialize other compounds which also target IL-23R outside of the Janssen License and Collaboration Agreement until completion of the Phase 2b portion of the Phase 2 clinical trial. We and Janssen are required to indemnify the other party against all losses and expenses related to breaches of its representations, warranties and covenants under the Janssen License and Collaboration Agreement.

The Janssen License and Collaboration Agreement remains in effect until the royalty obligations cease following patent and regulatory expiry, unless terminated earlier. Either we or Janssen may terminate the Janssen License and Collaboration Agreement for uncured material breach. Janssen retains the right to terminate the Janssen License and Collaboration Agreement for convenience and without cause on written notice of a certain period to us. Upon a termination of the Janssen License and Collaboration Agreement, all rights revert back to us, and in certain circumstances, if such termination occurs during ongoing clinical trials, Janssen would, if requested, provide certain financial and operational support to us for the completion of such trials.

Critical Accounting Polices 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.

Revenue Recognition

Effective July 1, 2017, we adopted Accounting Standards Codification, or ASC Topic 606, *Revenue from Contracts with Customers* ("ASC 606") using the full retrospective transition method. We did not have any effective contracts within the scope of this guidance prior to July 1, 2017. Accordingly, we did not elect to use any of the practical expedients permitted under the transition guidance, and the adoption had no impact on our previously reported financial position, results of operations or liquidity. This standard applies to all contracts with customers, except for contracts that are within the scope of other standards, such as leases, insurance, collaboration arrangements and financial instruments. Under ASC 606, we recognize revenue when our customer obtains control of promised goods or services, in an amount that reflects the consideration which we expect to receive in exchange for those goods or services. To determine revenue recognition for arrangements that we determine are within the scope of ASC 606, we perform the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) we satisfy a performance obligation. We only apply the five-step model to contracts when it is probable that we will collect the consideration we are entitled to in exchange for the goods or services it transfers to the customer. At contract inception, once the contract is determined to be within the scope of ASC 606, we assess the goods or services promised within each contract and determine those that are performance obligations and assess whether each

promised good or service is distinct. We then recognize as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

We entered into a license and collaboration agreement that became effective upon resolution of regulatory requirements during the third quarter of 2017 which is within the scope of ASC 606, under which we have licensed certain rights to our PTG-200 product candidate to a third party and may enter into other such arrangements in the future. The terms of the arrangement include payment to us of one or more of the following: non-refundable, up-front license fees, development and regulatory and commercial milestone payments, and royalties on net sales of licensed products.

Licenses of intellectual property: If the license to our intellectual property is determined to be distinct from the other performance obligation identified in the arrangement, we recognize revenue from non-refundable, up-front fees allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the license. For licenses that are bundled with other promises, we utilize judgment to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring proportional performance for purposes of recognizing revenue from non-refundable, up-front fees. We evaluate the measure of proportional performance each reporting period and, if necessary, adjust the measure of performance and related revenue recognition.

Milestone payments: At the inception of each arrangement that includes development, regulatory or commercial milestone payments, we evaluate whether the milestones are considered probable of being reached and estimate the amount to be included in the transaction price. ASC 606 suggests two alternatives to use when estimating the amount of variable consideration: the expected value method and the most likely amount method. Under the expected value method, an entity considers the sum of probability-weighted amounts in a range of possible consideration amounts. Under the most likely amount method, an entity considers the single most likely amount in a range of possible consideration amounts. Whichever method is used, it should be consistently applied throughout the life of the contract; however, it is not necessary for us to use the same approach for all contracts. We expect to use the most likely amount method for development and regulatory milestone payments. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within our control or the control of the licensee, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. The transaction price is then allocated to each performance obligation on a relative stand-alone selling price basis, for which we recognize revenue as or when the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, we re-evaluate the probability or achievement of each such milestone and any related constraint, and if necessary, adjust our estimates of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenues and earnings in the period of adjustment. To date, we have not recognized any milestone payments resulting from our collaboration arrangement.

Royalties: For arrangements that include sales-based royalties, including milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, we recognize revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). To date, we have not recognized any royalty revenue resulting from our collaboration arrangement.

Up-front payments and fees are recorded as deferred revenue upon receipt or when due and may require deferral of revenue recognition to a future period until we perform our obligations under these arrangements. Amounts payable to us are recorded as accounts receivable when our right to consideration is unconditional. We do not assess whether a contract has a significant financing component if the expectation at contract inception is such that the period between payment by the customer and the transfer of the promised goods or services to the customer will be one year or less.

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 statements 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.

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 fair value, and the resulting stock-based compensation expense, using the Black-Scholes option-pricing model. The estimated 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—Prior to our IPO in August 2016, we were privately held and did 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. We will continue to apply this process until a sufficient amount of historical information regarding the volatility of our own stock price becomes available.

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, 2017, 2016, and 2015, stock-based compensation expense was $4.2 million, $2.1 million and $99,000, respectively. As of December 31, 2017, we had $10.7 million of total unrecognized stock-based compensation costs, which we expect to recognize over a weighted-average period of 2.46 years.

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 all or some portion of a deferred tax asset will not be realized.

As of December 31, 2017, our total gross deferred tax assets were $25.9 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, 2017, our net operating loss carryforwards for federal income tax purposes of $79.2 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 $68.0 million which are available to offset future taxable income, if any, through 2033. As of December 31, 2017, we also had accumulated Australian tax losses of $10.4 million available for carry forward against future earnings, which under relevant tax laws do not expire but may not be available under certain circumstances.

On December 22, 2017, the Tax Cuts and Jobs Act of 2017 ("Tax Act") was signed into law making significant changes to the Internal Revenue Code. Changes include, but are not limited to, a corporate tax rate decrease from 35% to 21% effective for tax years beginning after December 31, 2017, the transition of U.S. international taxation from a worldwide tax system to a territorial system, and a one-time transition tax on the mandatory deemed repatriation of cumulative foreign earnings as of December 31, 2017.

The reduction of the corporate tax rate under the Tax Act is effective January 1, 2018. Consequently, we have recorded a decrease in net deferred tax assets of $11.5 million, with a corresponding adjustment to the valuation allowance of $11.5 million, for the year ended December 31, 2017. The state deferred tax effect on federal deferred tax assets has been calculated using 79% rather than the previous 66% federal benefit. The increase in deferred tax assets has been offset against an increase to the valuation allowance.

The Deemed Repatriation Transition Tax, ("Transition Tax") is a tax on previously untaxed accumulated and current earnings and profits ("E&P") of certain foreign subsidiaries. To determine the amount of the Transition Tax, we must determine, in addition to other factors, the amount of post-1986 E&P of the relevant subsidiaries, as well as the amount of non-U.S. income taxes paid on such earnings. Since Protagonist Pty Ltd., our foreign subsidiary, has a cumulative deficit in E&P, there is no Transition Tax to be included in the December 31, 2017 tax provision.

On December 22, 2017, the SEC staff issued Staff Accounting Bulletin No. 118 ("SAB 118"), which provides guidance for the tax effect of the Tax Act. SAB 118 provides a measurement period that should not extend beyond one year from the Tax Act's enactment date for companies to complete the accounting under Accounting Standards Codification Topic 740, *Income Taxes* ("ASC 740"). In accordance with SAB 118, we must reflect the income tax effects of those aspects of the Tax Act for which the accounting under ASC 740 is complete. To the extent that our accounting for certain income tax effects of the Tax Act is incomplete, but we are able to determine a reasonable estimate, we must record a provisional estimate in our consolidated financial statements. If we cannot determine a provisional estimate to be included in our consolidated financial statements, we should continue to apply ASC 740 on the basis of the provisions of the tax laws that were in effect immediately before the enactment of the Tax Act. The amounts of the tax effects related to the Tax Act described in the paragraphs above represent our reasonable estimates and are provisional amounts within the meaning of SAB 118. The provisional transition tax at zero has been determined based on the cumulative deficit foreign E&P as of the relevant measurement date. Any change in such estimate during the measurement period should have no impact on our financial statements. Also, it is expected that the U.S. Treasury will issue regulations and other guidance on the application of certain provisions of the Tax Act. In subsequent periods, but within the measurement period, we will analyze that guidance and other necessary information to refine our estimates and complete our accounting for the tax effects of the Tax Act as necessary.

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 (the "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. Based on a review of our equity transactions since inception, we believe a portion of our net operating loss carryforwards and credit carryforwards may be limited due to an equity financing that occurred in 2015.

Recent Accounting Pronouncements

Information regarding recent accounting pronouncements applicable to us is included in the notes to our consolidated financial statements included elsewhere in this Annual Report.

Components of Our Results of Operations

License and Collaboration Revenue

Our license and collaboration revenue is derived from payments we receive under the Janssen License and Collaboration Agreement.

We identified the following material promises under the Janssen License and Collaboration Agreement: (1) the license related to PTG-200, (2) the performance of development services, including regulatory support, during Phase 1 clinical trial for PTG-200 through the filing of the IND by Janssen, and (3) compound supply services for Phase 1 and Phase 2 activities. We considered that the license has standalone functionality and is capable of being distinct. However, we determined that the license is not distinct from the development and compound supply services within the context of the agreement because the development and compound supply services significantly increase the utility of the intellectual property.

Specifically, our development, manufacturing and commercialization license can provide benefit to Janssen only in combination with our development services in the Phase 1 study. The intellectual property ("IP") related to the peptide technology platform, which is proprietary to us, is the foundation for the development activities related to the treatment for CD. The compound supply services are a necessary and integral part of the development services as they could only be conducted utilizing the outcomes of these services. Given the development services under the Janssen Collaboration Agreement are expected to involve significant further development of the initial IP, we have concluded that the development and compound supply services are not distinct from the license, and thus the license, development services and compound supply services are combined into a single performance obligation. The nature of the combined performance obligation is to provide development and compound supply services to Janssen under the arrangement.

We also evaluated whether the fees related to the First Opt-in Election and Second Opt-in Election are options with material rights. These two options include additional sublicense rights and patent rights transferred to Janssen upon exercising both of these options. We concluded that Janssen's opt in rights are not options with material rights because the $50.0 million upfront payment to us was not negotiated to provide incremental discount for the future opt in payments at the end of Phase 2a and Phase 2b. The option to "opt in" provides Janssen with a license for IP that has been improved from the license initially granted for a term in the case of the opt in after completion Phase 2a and then a perpetual license in the case of opt in after completion of Phase 2b. Therefore, the First Opt-in Election and Second Opt-in Election options are not considered to be material rights. The option fees will be recognized as revenue when, and if, Janssen exercises its options because we have no further performance obligations at that point.

For revenue recognition purposes, we determined that the duration of the contract begins on the effective date of July 13, 2017 and ends upon completion of Phase 2a activities. The contract duration is defined as the period in which parties to the contract have present enforceable rights and obligations. We analyzed the impact of Janssen terminating the agreement prior to the completion of Phase 2a and determined that there were significant economic penalties to

Janssen for doing so. We believe that if Janssen terminates the agreement upon completion of Phase 2a, the forfeiture of the remaining license rights and payment of 50% of the remaining Phase 2 costs is not a significant economic penalty when compared to paying $125 million as an opt in license fee to continue the use of the License. Thus, the duration of the contract is limited to the end of Phase 2a.

We determined that the transaction price of the Janssen License and Collaboration Agreement was $53.9 million as of December 31, 2017, a decrease of $0.4 million from the transaction price of $54.3 million that was determined at September 30, 2017. In order to determine the transaction price, we evaluated all the payments to be received during the duration of the contract. We determined that the $50.0 million upfront payment, the $25.0 million payment payable upon filing of the Phase 2 IND, which is fully constrained as of December 31, 2017, and $3.9 million of estimated variable consideration for cost-sharing payments from Janssen for agreed upon services related to Phase 2 activities constituted consideration to be included in the transaction price, which is to be allocated to the combined performance obligation. The decrease in the transaction price from September 30, 2017 was due to a decrease in variable consideration related to compound supply services. We will re-evaluate the transaction price in each reporting period and as uncertain events are resolved or other changes in circumstances occur.

As part of the evaluation for determining that the $25.0 million payment upon filing of Phase 2 IND is fully constrained as of December 31, 2017, we considered several factors, including the stage of development of PTG-200 and that achievement of the milestone is outside of our control, and concluded that the filing of the Phase 2 IND is not probable at this time. If and when the filing of the Phase 2 IND becomes probable, the $25.0 million payment will be constrained by contra revenue amounts for payments that we expect to make for 20% of the cost of Phase 2 activities to be performed by Janssen. The additional potential development, regulatory and sales milestone payments of up to an aggregate of $590.0 million after the completion of Phase 2a activities that we are eligible to receive are outside the contract term and as such have been excluded from the transaction price. Any consideration related to sales-based milestones (including royalties) will be recognized when the related sales occur as they were determined to relate predominantly to the license granted to Janssen and therefore have also been excluded from the transaction price. At the end of each reporting period, we will update our assessment of whether an estimate of variable consideration is constrained and update the estimated transaction price accordingly.

Variable consideration for cost-sharing payments related to agreed upon services for Phase 2 activities that we perform within the duration of the contract are included in the transaction price at an amount equal to 80% of the estimated budgeted costs for these activities, including primarily internal full-time equivalent effort and third party contract costs. We are responsible for 20% of the development costs for the Phase 2 clinical trial. Accordingly, a significant portion of this work is expected to be performed by Janssen. Because the Phase 2 clinical trial activity is related to the license, it is not capable of being distinct. This is because both we and Janssen cannot benefit from these activities absent the Phase 1 activities. As the Phase 2 activities for which we will share 20% of the cost activities are not capable of being distinct and are not separately identifiable within the context of the contract, they are not a distinct service that Janssen transfers us. Therefore, the consideration payable to Janssen is accounted for as a reduction in the transaction price. We and Janssen make quarterly cost-sharing payments to one another in amounts necessary to ensure that each party bears its contractual share of the overall shared costs incurred. We account for cost-sharing payments from Janssen as increases in license and collaboration revenue in our consolidated statements of operations, while cost-sharing payments to Janssen are accounted for as reductions in license and collaboration revenue, or contra-revenue. Costs we incur related to agreed upon services for Phase 2 activities under the Janssen License and Collaboration Agreement are recorded as research and development expenses in our consolidated statements of operations.

In summary, the license, the development activities for Phase 1 activities and the agreed upon services for Phase 2 activities are combined as one performance obligation that will be performed over the duration of the contract, which is from the effective date of the Janssen License and Collaboration Agreement through to the completion of Phase 2a activities. Since we have determined that the combined performance obligation is satisfied over time, ASC 606 requires us to select a single revenue recognition method for the performance obligation that faithfully depicts our performance in transferring control of the services. The guidance allows entities to choose between two methods to measure its progress toward complete satisfaction of a performance obligation:

1. Output methods - recognize revenue on the basis of direct measurements of the value to the customer of the goods or services transferred to date relative to the remaining goods or services promised under the contract (e.g. surveys of performance completed to date, appraisals of results achieved, milestones reached, time elapsed, and units of produced or units delivered); and

2. Input methods - recognize revenue on the basis of the entity's efforts or inputs to the satisfaction of a performance obligation (e.g., resources consumed, labor hours expended, costs incurred, or time elapsed) relative to the total expected inputs to the satisfaction of that performance obligation.

We concluded that we will utilize a cost-based input method to measure proportional performance and to calculate the corresponding amount of revenue to recognize. We believe this is the best measure of progress because other measures do not reflect how we transfer our performance obligation to Janssen. In applying the cost-based input methods of revenue recognition, we use actual costs incurred relative to budgeted costs to fulfill the combined performance obligation. These costs consist primarily of internal full-time equivalent effort and third-party contract costs. Revenue will be recognized based on actual costs incurred as a percentage of total budgeted costs as we complete our performance obligations, which we believe will be fulfilled within the next 12 months. A cost-based input method of revenue recognition requires management to make estimates of costs to complete our performance obligations. In making such estimates, significant judgment is required to evaluate assumptions related to cost estimates. The cumulative effect of revisions to estimated costs to complete our performance obligations will be recorded in the period in which changes are identified and amounts can be reasonably estimated. A significant change in these assumptions and estimates could have a material impact on the timing and amount of revenue recognized in future periods.

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 unless there is an alternative future use in other research and development projects or otherwise. Non-refundable advance payments for goods and services that will be used in future research and development activities are expensed when the activity has been performed or when the goods have been received rather than when payment has been made. In instances where we enter into agreements with third parties to provide research and development services to us, costs are expensed as services are performed. Amounts due under such arrangements may be either fixed fee or fee for service and may include upfront payments, monthly payments, and payments upon the completion of milestones or the receipt of deliverables.

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;

- license fees and milestone payments under license and collaboration agreements; 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 grants under government programs as a reduction of research and development expenses when the related research costs are incurred. In addition, we recognize the funds related to our Australian research and development tax incentive that are not subject to refund provisions as a reduction of research and development expenses. 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. The Australian research and development tax incentive is 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 and indirect costs incurred to product candidates when they enter clinical development. For product candidates in clinical development, direct costs consist primarily of clinical, pre-clinical, and drug discovery costs, costs of supplying drug substance and drug product for use in clinical and pre-clinical studies, including clinical manufacturing costs, contract research organization fees, and other contracted services pertaining to specific clinical and pre-clinical studies. Indirect costs allocated to our product candidates on a program specific basis include research and development employee salaries, benefits, and stock-based compensation, and indirect overhead and other administrative support costs. Program-specific costs are unallocated when the 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 provide financial information regarding the costs incurred for early stage pre-clinical and drug discovery programs on a program-specific basis prior to the clinical development stage. We initiated a Phase 1 clinical study of PTG-300 during the second quarter of 2017. We have presented separately in the table below costs associated with the PTG-300 program beginning in June 2017. We initiated a Phase 1 clinical study of PTG-200 during the fourth quarter of 2017. We have presented separately in the table below costs associated with the PTG-200 program beginning in December 2017. Our development and compound supply expenses incurred under the Janssen License and Collaboration Agreement prior to December 2017 are included in pre-clinical and drug discovery research expense.

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

	Year Ended December 31,		
	2017	2016	2015
	(In thousands)		
Clinical and development expense — PTG-100	$ 25,825	$ 17,738	$ 1,563
Clinical and development expense — PTG-200	2,079	—	—
Clinical and development expense — PTG-300	4,246	—	—
Pre-clinical and drug discovery research expense	15,292	11,849	11,159
Milestone payment obligation to former collaboration partner	250	250	—
Less: Reimbursement of expenses under grants and incentives	(1,511)	(4,132)	(891)
Total research and development expenses	$ 46,181	$ 25,705	$ 11,831

We expect our research and development expenses will increase as we progress our product candidates, including development activities under the Janssen License and Collaboration Agreement, 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 our 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. Our research and development programs may be subject to change from time to time as we evaluate our priorities and available resources.

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, information technology, depreciation and amortization expense and other supplies. We expect to incur additional expenses to support the growth of our operations and as a result of operating as a public company, including expenses related to compliance with the rules and regulations of the SEC, and those of the 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

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.

In connection with our Series C redeemable convertible preferred stock financing, we were obligated to sell additional shares of Series C redeemable convertible preferred stock in a subsequent closing 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 fair value on the date of issuance, and we remeasured the liability on each subsequent balance sheet date. 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 and the liability was reclassified to redeemable convertible preferred stock.

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 accounted for these warrants as a liability in our condensed consolidated financial statements because the underlying instrument into which the warrants were exercisable contained redemption provisions that were outside our control. Upon the exercise of warrants in April 2016, the fair value of the redeemable convertible preferred stock warrant liability was remeasured and the liability was reclassified to redeemable convertible preferred stock. The remaining warrants expired unexercised in May 2016 and, accordingly, are no longer subject to remeasurement.

Results of Operations

Comparison of the year ended December 31, 2017 and 2016

	Year Ended December 31,		Dollar Change	% Change
	2017	2016		
	(Dollars in thousands)			
License and collaboration revenue - related party	$ 20,063	$ —	$ 20,063	100
Operating expenses:				
Research and development [1]	46,181	25,705	$ 20,476	80
General and administrative [2]	11,779	6,961	4,818	69
Total operating expenses	57,960	32,666	25,294	77
Loss from operations	(37,897)	(32,666)	(5,231)	16
Interest income	940	242	698	288
Change in fair value of redeemable convertible preferred stock tranche and warrant liabilities	—	(4,719)	4,719	*
Other expense	—	(34)	34	*
Net loss	$ (36,957)	$ (37,177)	$ 220	1

(1) Includes $2.0 million and $1.1 million of non-cash stock-based compensation expense for the year ended December 31, 2017 and 2016, respectively.
(2) Includes $2.2 million and $1.0 million of non-cash stock-based compensation expense for the year ended December 31, 2017 and 2016, respectively.
* *Percentage not meaningful*

License and Collaboration Revenue

For the year ended December 31, 2017, we recognized $20.1 million as license and collaboration revenue under the Janssen License and Collaboration Agreement. This amount included $19.0 million of the transaction price for the Janssen License and Collaboration Agreement recognized based on proportional performance as measured by actual costs incurred as a percentage of budgeted costs, and $1.1 million for other services related to Phase 2 activities performed by us on behalf of Janssen that are not included in the performance obligations identified under the Janssen License and Collaboration Agreement. We did not recognize any license and collaboration revenue during the year ended December 31, 2016.

Deferred revenue related to the Janssen License and Collaboration Agreement was $31.8 million as of December 31, 2017 and was comprised of the $50.0 million upfront payment and $0.7 million of cost sharing payments from Janssen for agreed upon services for Phase 2 activities, less $19.0 million of license and collaboration revenue recognized under the contract. We recorded a $1.8 million receivable from collaboration partner as of December 31, 2017 for cost sharing amounts payable from Janssen.

Research and Development Expenses

Research and development expenses increased $20.5 million, or 80%, from $25.7 million for the year ended December 31, 2016, to $46.2 million for the year ended December 31, 2017. The increase was primarily due to an increase of $8.1 million in PTG-100 clinical trial and development expenses, $2.1 million for PTG-200 Phase 1 clinical trial and development expenses, $4.2 million for PTG-300 Phase 1 clinical trial and development expenses, an increase of $3.5 million in pre-clinical and discovery research expense, including pre-clinical development activities for PTG-200, PTG-300 and our other product candidates, and a decrease of $2.6 million in expense reimbursement under grants and incentives. Research and development expenses for the year ended December 31, 2017 include an increase in personnel costs due to increased research and development headcount from 27 employees at December 31, 2016 to 44 employees at December 31, 2017.

General and Administrative Expenses

General and administrative expenses increased $4.8 million, or 69%, from $7.0 million for the year ended December 31, 2016, to $11.8 million for the year ended December 31, 2017. The increase was primarily due to an increase of $2.7 million in personnel costs to support the growth of our operations and increases of $1.1 million in professional service fees and $1.0 million in consulting and contracted labor expenses due to the growth of our operations and operating as a public company.

Interest Income

Interest income increased $0.7 million, or 288%, from $0.2 million for the year ended December 31, 2016 to $0.9 million for the year ended December 31, 2017. The increase was primarily due to the investment of funds from our IPO in August 2016, the $50.0 million upfront payment from Janssen during the third quarter of 2017, and funds from our follow-on public offering of common stock during the fourth quarter of 2017.

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 and warrant liabilities was a charge of $4.7 million for the year ended December 31, 2016 due to the settlement of Series C

redeemable convertible preferred stock tranche liability in March 2016 and the fair value remeasurement of the outstanding warrant liability. There were no such items for the year ended December 31, 2017.

Comparison of the years ended December 31, 2016 and 2015

	Year Ended December 31,		Dollar	%
	2016	2015	Change	Change
	(Dollars in thousands)			
Operating expenses:				
Research and development [1]	$ 25,705	$ 11,831	$ 13,874	117
General and administrative [2]	6,961	2,963	3,998	135
Total operating expenses	32,666	14,794	17,872	121
Loss from operations	(32,666)	(14,794)	(17,872)	121
Interest income	242	19	223	*
Change in fair value of redeemable convertible preferred stock tranche and warrant liabilities	(4,719)	(83)	(4,636)	*
Other expense	(34)	—	(34)	100
Net loss	$ (37,177)	$ (14,858)	$ (22,319)	150

[1] Includes $1.1 million and $39,000 of non-cash stock-based compensation expense for the year ended December 31, 2016 and 2015, respectively.
[2] Includes $1.0 million and $60,000 of non-cash stock-based compensation expense for the year ended December 31, 2016 and 2015, respectively.
* *Percentage not meaningful*

Research and Development Expenses

Research and development expenses increased $13.9 million, or 117%, from $11.8 million for the year ended December 31, 2015 to $25.7 million for the year ended December 31, 2016. The increase was primarily due to an increase of $6.5 million related to contract manufacturing activities for PTG-100 clinical trials and other product candidate studies, an increase of $2.8 million in costs for third party consultants, an increase of $2.7 million in pre-clinical activities for our product candidates, an increase of $2.6 million in salaries and employee-related expense due to an increase in headcount, an increase of $1.9 million in PTG-100 Phase 1 clinical trials and other related studies, an increase of $0.3 million due to achieving certain development milestones in a prior collaboration agreement related to the initiation of preclinical development studies on PTG-300 and an increase of $0.3 million in facility expenses. The increases were partially offset by an increase of $3.3 million in government programs recognized as a reduction of research and development expenses, primarily due to the increase in our Australian research and development tax incentive including the recognition of amounts related to overseas finding that are no longer deemed to be at risk of clawback and funds earned under the Small Business Research grant awards.

General and Administrative Expenses

General and administrative expenses increased $4.0 million, or 135%, from $3.0 million for the year ended December 31, 2015, to $7.0 million for the year ended December 31, 2016. The increase was primarily due to an increase of $1.9 million in professional service fees, an increase of $1.8 million increase in salaries and employee-related expense due to an increase in headcount to support the growth of our operations and an increase of $0.3 million in facility and other administrative expenses.

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

Change in fair value of redeemable convertible preferred stock tranche liability and warrant liabilities increased from a charge of $0.1 million for the year ended December 31, 2015 to a charge of $4.7 million for the year ended

December 31, 2016. The change was due to the fair value remeasurement of the outstanding mark to market liabilities as the fair value increased in 2016.

Liquidity and Capital Resources

Liquidity and Capital Expenditures

As of December 31, 2017, we had $155.5 million of cash, cash equivalents and available-for-sale securities and an accumulated deficit of $101.6 million. Our operations have been financed by net proceeds from the sale of shares of our capital stock and revenue from the Janssen License and Collaboration Agreement. During the third quarter of 2017 we became eligible for and received a non-refundable, upfront cash payment of $50.0 million from Janssen.

In September 2017, we filed a registration statement on Form S-3 with the Securities and Exchange Commission (File No. 333-220314), effective as of October 5, 2017, which permits the offering, issuance, and sale by us of up to a maximum aggregate offering price of $200.0 million of our common stock. Up to a maximum of $50.0 million of the maximum aggregate offering price of $200.0 million may be issued and sold pursuant to an at-the-market financing facility under a sales agreement with Cantor Fitzgerald & Co. (the "Sales Agreement").

As of the filing of this Annual Report, we have not sold any shares of our common stock pursuant to the Sales Agreement. In October 2017, we completed an underwritten public offering of 3,530,000 shares of our common stock at a public offering price of $17.00 per share. In November 2017, we issued an additional 529,500 shares of our common stock at a price of $17.00 per share following the underwriters' exercise of their option to purchase additional shares. Net proceeds, after deducting underwriting commissions and offering costs, were $64.5 million. As of the filing of this Annual Report, up to a maximum aggregate offering price of $131.0 million of our common stock may be offered, issued and sold by us under our registration statement on Form S-3.

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 and available-for-sale securities will be sufficient to meet our anticipated operating and capital expenditure requirements for at least the next 12 months from the date of this filing. 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. 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 potential 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, but such financing may not be available at terms acceptable to us, if at all. 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 and ability to obtain 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 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 achievement of development, regulatory and sales milestones resulting in payments to us from Janssen under the Janssen License and Collaboration Agreement, and the timing of receipt of such payments, if any;
- the timing, receipt and amount of royalties under the Janssen License and Collaboration Agreement on worldwide net sales of PTG-200, upon regulatory approval or clearance, if any;

- 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;
- costs necessary 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 or convertible debt securities, 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 and, with the exception of payments we may receive under the Janssen License and Collaboration Agreement, we do not currently have any commitments for future external financing. 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,		
	2017	2016	2015
	(In thousands)		
Cash provided by (used in) operating activities	$ 3,872	$ (29,972)	$ (14,385)
Cash provided by (used in) investing activities	15,823	(59,328)	(8,264)
Cash provided by financing activities	65,554	106,307	17,419

Cash Flows from Operating Activities

Cash provided by operating activities for the year ended December 31, 2017 was $3.9 million, consisting of a net change of $35.6 million in net operating assets and liabilities and non-cash charges of $5.3 million, partially offset by our net loss of $37.0 million. The change in net operating assets and liabilities was due primarily to an increase of $31.8 million in deferred revenue related to the Janssen License and Collaboration Agreement, an increase of $4.8 million in accounts payable and accrued expenses related primarily to an increase in research and development activities and other general and administrative professional services and a decrease of $1.1 million in the Australian research and development tax incentive receivable, partially offset by an increase of $1.8 million in receivable from collaboration partner and an increase of $0.3 million in prepaid expenses and other assets. The non-cash charges were primarily comprised of $4.2 million of stock-based compensation, $0.7 million of net amortization of premium on available-for-sale securities and $0.4 million of depreciation and amortization.

Cash used in operating activities for the year ended December 31, 2016 was $30.0 million, consisting of a net loss of $37.2 million and a net change of $0.1 million in our net operating assets and liabilities, which were offset by non-cash charges of $7.3 million. The non-cash charges were primarily comprised of $4.2 million for the change in fair value associated with redeemable convertible preferred stock tranche liability, $2.1 million for stock-based compensation, $0.5 million for the change in fair value of convertible preferred stock warrant liability, and $0.3 million for depreciation and amortization expense. The change in our net operating assets and liabilities was due primarily to an increase of $1.8 million in prepaid and other current assets related to advance payments of costs for research activities during the current period and an increase of $1.6 million in the receivable related to the Australian research and development tax

incentives, offset by a $3.3 million increase in our accounts payable and accrued expenses and other payables related to an 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 Flows from Investing Activities

Cash provided by investing activities for the year ended December 31, 2017 was $15.8 million, consisting of proceeds from maturities of available-for-sale securities of $56.0 million, partially offset by purchases of available-for-sale securities of $39.5 million and purchases of property and equipment of $0.7 million. Purchases of property and equipment were primarily related to purchases of scientific equipment.

Cash used in investing activities for the year ended December 31, 2016 was $59.3 million, consisting of purchases of available-for-sale securities of $73.2 million and purchases of property and equipment of $0.4 million, partially offset by proceeds from maturities of our available-for-sale securities of $14.2 million. Purchases of property and equipment were primarily related to the expansion of our laboratory and related equipment.

Cash used in investing activities for the year 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. Purchases of property and equipment were primarily related to the expansion of our laboratory and related equipment.

Cash Flows from Financing Activities

Cash provided by financing activities for the year ended December 31, 2017 was $65.5 million, consisting of net proceeds of $64.5 million from our public offering of common stock and proceeds of $1.0 million from the issuance of common stock upon exercise of stock options and purchases of common stock under our employee stock purchase plan.

Cash provided by financing activities for the year ended December 31, 2016 was $106.3 million, consisting of net proceeds of $83.6 million from our initial public offering, net proceeds of $22.5 million from the issuance of redeemable convertible preferred stock and proceeds of $0.2 million from the issuance of common stock upon exercise of stock options.

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

Contractual Obligations and Other Commitments

In March 2017, we entered into a lease agreement for office and laboratory space in Newark, California. We relocated our operations to the new facility in May 2017. We provided the landlord with a $450,000 letter of credit collateralized by restricted cash as security deposit for the lease which expires in May 2024. Under the terms of the lease, we are responsible for certain taxes, insurance and maintenance expenses.

The following table summarizes our future minimum contractual obligations as of December 31, 2017:

	Payments Due by Period				
Contractual Obligations:	**Less Than 1 Year**	**1 to 3 Years**	**More Than 3 to 5 Years**	**5 Years**	**Total**
			(In thousands)		
Operating lease obligations	$ 1,667	$ 3,941	$ 4,181	$3,106	$12,895
Total contractual obligations	$ 1,667	$ 3,941	$ 4,181	$3,106	$12,895

Potential Obligations Not Included in the Table Above

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. Future potential payments under these agreements are not included in the table above.

Under the Janssen License and Collaboration Agreement, we share with Janssen certain development, regulatory and compound supply costs. The actual amounts that we pay Janssen or that Janssen pays us will depend on numerous factors, some of which are outside of our control and some of which are contingent upon the success of certain development and regulatory activities. Future development and commercialization payments to Janssen are not included in the table above as the timing and amounts of such payments are not determinable.

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. The nomination of PTG-300 as a development candidate triggered a $250,000 payment from us to Zealand, which was recognized within research and development expense in our consolidated statement of operations for the year ended December 31, 2016. The initiation of a Phase 1 clinical trial for PTG-300 triggered a $250,000 payment from us to Zealand, which was recognized within research and development expense in our consolidated statement of operations for the year ended December 31, 2017. 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. Future development, regulatory and sales payments to Zealand are not included in the table above as the timing and amounts of such payments are not determinable.

Off-Balance Sheet Arrangements

We have not entered into any off-balance sheet arrangements, as defined under SEC rules, including the use of structured finance, special purpose entities or variable interest entities.

Item 7A.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 $155.5 million and $87.7 million in cash, cash equivalents and available-for-sale securities at December 31, 2017 and December 31, 2016, respectively. Cash and cash equivalents consist of cash, money market funds, commercial paper and government bonds. Available-for-sale securities consist of corporate bonds, commercial paper and government bonds. Short-term available-for-sale securities have maturities of greater than three months but no longer than 365 days as of the balance sheet date. Long-term available-for-sale securities have maturities of 365 days or longer

as of the balance sheet date. Such interest earning instruments carry a degree of interest rate risk; however, historical fluctuations in interest income have not been material. We had no outstanding debt as of December 31, 2017.

Approximately $1.2 million and $1.9 million of our cash balance was located in Australia at December 31, 2017 and December 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 becomes more significant. A 10% increase or decrease in current exchange rates would not have a material effect on our results of operations.

Item 8. Financial Statements and Supplementary Data

PROTAGONIST THERAPEUTICS, INC.

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Board of Directors and Stockholders of
Protagonist Therapeutics, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Protagonist Therapeutics, Inc. and its subsidiary as of December 31, 2017 and 2016, and the related consolidated statements of operations, comprehensive loss, redeemable convertible preferred stock and stockholders' equity (deficit) and cash flows for each of the three years in the period ended December 31, 2017, including the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2017 and 2016, and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2017 in conformity with accounting principles generally accepted in the United States of America.

Basis for Opinion

These consolidated financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's consolidated financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) ("PCAOB") and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits of these consolidated financial statements in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the consolidated financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the consolidated financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the consolidated financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the consolidated financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ PricewaterhouseCoopers LLP

San Jose, California
March 7, 2018

We have served as the Company's auditor since 2015.

PROTAGONIST THERAPEUTICS, INC.
Consolidated Balance Sheets
(In thousands, except share data)

	December 31, 2017	December 31, 2016
Assets		
Current assets:		
Cash and cash equivalents	$ 106,029	$ 21,084
Restricted cash - current	10	10
Available-for-sale securities - current	37,972	56,515
Receivable from collaboration partner - related party	1,816	—
Research and development tax incentive receivable	1,347	2,241
Prepaid expenses and other current assets	3,773	3,394
Total current assets	150,947	83,244
Property and equipment, net	879	562
Restricted cash - noncurrent	450	—
Available-for-sale securities - noncurrent	11,458	10,150
Other assets	—	34
Total assets	$ 163,734	$ 93,990
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 1,257	$ 1,163
Accrued expenses and other payables	9,546	5,272
Deferred revenue - related party	31,752	—
Total current liabilities	42,555	6,435
Deferred rent - noncurrent	547	—
Total liabilities	43,102	6,435
Commitments and contingencies (Note 8)		
Stockholders' equity:		
Preferred stock, $0.00001 par value, 10,000,000 shares authorized; no shares issued and outstanding	—	—
Common stock, $0.00001 par value, 90,000,000 shares authorized; 21,088,306 and 16,722,280 shares issued and outstanding as of December 31, 2017 and 2016, respectively	—	—
Additional paid-in capital	222,188	152,393
Accumulated other comprehensive loss	(6)	(245)
Accumulated deficit	(101,550)	(64,593)
Total stockholders' equity	120,632	87,555
Total liabilities and stockholders' equity	$ 163,734	$ 93,990

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,		
	2017	2016	2015
License and collaboration revenue - related party	$ 20,063	$ —	$ —
Operating expenses:			
Research and development	46,181	25,705	11,831
General and administrative	11,779	6,961	2,963
Total operating expenses	57,960	32,666	14,794
Loss from operations	(37,897)	(32,666)	(14,794)
Interest income	940	242	19
Change in fair value of redeemable convertible preferred stock tranche and warrant liabilities	—	(4,719)	(83)
Other expense	—	(34)	—
Net loss	$ (36,957)	$ (37,177)	$ (14,858)
Net loss attributable to common stockholders	$ (36,957)	$ (37,735)	$ (14,933)
Net loss per share attributable to common stockholders, basic and diluted	$ (2.09)	$ (5.80)	$ (59.32)
Weighted-average shares used to compute net loss per share attributable to common stockholders, basic and diluted	17,694,505	6,501,796	251,717

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,		
	2017	2016	2015
Net loss	$ (36,957)	$ (37,177)	$ (14,858)
Other comprehensive loss:			
Gain (loss) on translation of foreign operations	298	(76)	3
Unrealized loss on available-for-sale securities	(59)	(67)	(5)
Comprehensive loss	$ (36,718)	$ (37,320)	$ (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' Equity (Deficit)
(In thousands, except share and per share data)

	Redeemable Convertible Preferred Stock		Common Stock		Additional Paid-In Capital	Accumulated Other Comprehensive Gain (Loss)	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount				
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)
Issuance of Series C redeemable convertible preferred stock, net of issuance costs	45,189,794	22,488	—	—	—	—	—	—
Settlement of fair value of redeemable convertible preferred stock tranche liability	—	5,837	—	—	—	—	—	—
Exercise of redeemable convertible preferred stock warrant liability	1,999,998	1,025	—	—	—	—	—	—
Accretion of redemption of convertible preferred stock to redemption value	—	558	—	—	(558)	—	—	(558)
Conversion of redeemable convertible preferred stock to common stock at closing of initial public offering	(124,374,909)	(66,904)	8,577,571	—	66,904	—	—	66,904
Issuance of common stock upon initial public offering, net of issuance costs	—	—	7,752,972	—	83,648	—	—	83,648
Stock-based compensation expense	—	—	—	—	2,130	—	—	2,130
Issuance of common stock upon the exercise of options	—	—	119,328	—	151	—	—	151
Other comprehensive loss	—	—	—	—	—	(143)	—	(143)
Net loss	—	—	—	—	—	—	(37,177)	(37,177)
Balance at December 31, 2016	—	—	16,722,280	—	152,393	(245)	(64,593)	87,555
Issuance of common stock upon public offering, net of issuance costs	—	—	4,059,500	—	64,547	—	—	64,547
Stock-based compensation expense	—	—	—	—	4,241	—	—	4,241
Issuance of common stock upon the exercise of options and purchases under employee stock purchase plan	—	—	306,526	—	1,007	—	—	1,007
Other comprehensive gain	—	—	—	—	—	239	—	239
Net loss	—	—	—	—	—	—	(36,957)	(36,957)
Balance at December 31, 2017	—	$ —	21,088,306	$ —	$ 222,188	$ (6)	$ (101,550)	$ 120,632

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,		
	2017	2016	2015
CASH FLOWS FROM OPERATING ACTIVITIES			
Net loss	$ (36,957)	$ (37,177)	$ (14,858)
Adjustments to reconcile net loss to net cash provided by (used in) operating activities:			
Stock-based compensation	4,241	2,130	99
Net amortization of premium on available-for-sale securities	687	117	(8)
Depreciation and amortization	406	317	247
(Gain) loss on disposal of property and equipment	(62)	34	—
Change in fair value associated with redeemable convertible preferred stock tranche liability	—	4,194	626
Change in fair value of redeemable convertible preferred stock warrant liability	—	525	(543)
Changes in operating assets and liabilities:			
Research and development tax incentive receivable	1,070	(1,588)	(192)
Receivable from collaboration partner - related party	(1,816)	—	—
Prepaid expenses and other assets	(333)	(1,804)	(1,532)
Accounts payable	91	(115)	898
Accrued expenses and other payables	4,793	3,395	878
Deferred revenue - related party	31,752	—	—
Net cash provided by (used in) operating activities	3,872	(29,972)	(14,385)
CASH FLOWS FROM INVESTING ACTIVITIES			
Purchase of available-for-sale securities	(39,546)	(73,169)	(7,865)
Proceeds from maturities of available-for-sale securities	56,035	14,188	—
Purchases of property and equipment, net	(666)	(347)	(399)
Net cash provided by (used in) investing activities	15,823	(59,328)	(8,264)
CASH FLOWS FROM FINANCING ACTIVITIES			
Proceeds from issuance of common stock, net of issuance costs	64,547	83,648	—
Proceeds from issuance of common stock upon exercise of stock options and purchases under employee stock purchase plan	1,007	151	57
Proceeds from issuance of redeemable convertible preferred stock, net of issuance costs	—	22,508	17,362
Net cash provided by financing activities	65,554	106,307	17,419
Effect of exchange rate changes on cash, cash equivalents and restricted cash	146	22	(39)
Net increase (decrease) in cash, cash equivalents and restricted cash	85,395	17,029	(5,269)
Cash, cash equivalents and restricted cash, beginning of year	21,094	4,065	9,334
Cash, cash equivalents and restricted cash, end of year	$ 106,489	$ 21,094	$ 4,065
SUPPLEMENTAL DISCLOSURES OF NON-CASH FINANCING INFORMATION:			
Acquisition of new equipment upon trade-in for existing equipment	$ 185	$ —	$ —
Deferred offering costs in accounts payable and accrued liabilities	$ 66	$ —	$ —
Conversion of redeemable convertible preferred stock to common stock at closing of initial public offering	$ —	$ 66,904	$ —
Settlement of fair value of redeemable convertible preferred stock liability	$ —	$ 5,837	$ —
Reclassification of preferred stock warrant liability to equity	$ —	$ 1,005	$ —
Accretion of redeemable convertible preferred stock	$ —	$ 558	$ 75
Purchases of property and equipment in accounts payable	$ —	$ 21	$ —
Tranche liability in connection with the Series C redeemable convertible preferred stock financing	$ —	$ —	$ 1,017

The accompanying notes are an integral part of these consolidated financial statements.

PROTAGONIST THERAPEUTICS, INC.
Notes to Consolidated Financial Statements

Note 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 Newark, California. The Company is a clinical-stage biopharmaceutical company with a proprietary technology platform that enables the discovery and development of novel constrained peptide-based drug candidates that address significant unmet medical needs. Protagonist Pty Limited ("Protagonist Australia") is a wholly-owned subsidiary of the Company and is located in Brisbane, Queensland, Australia. Protagonist Australia was incorporated in Australia in September 2001. The Company 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 the Company's common stock and Series A preferred stock. The Company manages its operations as a single operating segment.

Liquidity

The Company has incurred net losses from operations since inception and has an accumulated deficit of $101.6 million as of December 31, 2017. The Company's ultimate success depends on the outcome of its research and development activities. The Company expects to incur additional losses in the future and it anticipates the need to raise additional capital to fully implement its business plan. Through December 31, 2017, the Company has financed its operations through private placements of redeemable convertible preferred stock, an initial public offering ("IPO") of common stock, payments received under a license and collaboration agreement, and a follow-on public offering of common stock.

On August 10, 2016, the Company's registration statement on Form S-1 (File Nos. 333-212476 and 333-213071) related to its IPO became effective. The IPO closed on August 16, 2016, at which time the Company issued 7,500,000 shares of its common stock at a price of $12.00 per share. In addition, upon closing the IPO, all outstanding shares of the Company's redeemable convertible preferred stock converted into 8,577,571 shares of common stock. There were no shares of redeemable convertible preferred stock outstanding at December 31, 2017 or 2016. In September 2016, the Company issued an additional 252,972 shares of its common stock at a price of $12.00 per share following the underwriters' exercise of their option to purchase additional shares. The Company received an aggregate of $83.6 million in cash, net of underwriting discounts and commissions, after deducting offering costs paid by the Company.

In September 2017, the Company filed a registration statement on Form S-3 with the Securities and Exchange Commission ("SEC") (File No. 333-220314), effective as of October 5, 2017, which permits the offering, issuance, and sale by the Company of up to a maximum aggregate offering price of $200.0 million of its common stock. Up to a maximum of $50.0 million of the maximum aggregate offering price of $200.0 million may be issued and sold pursuant to an at-the-market financing facility under a sales agreement with Cantor Fitzgerald & Co. (the "Sales Agreement").

During 2017, the Company did not sell any shares of its common stock pursuant to the Sales Agreement. In October 2017, the Company completed an underwritten public offering of 3,530,000 shares of common stock at a public offering price of $17.00 per share. In November 2017, the Company issued an additional 529,500 shares of its common stock at a price of $17.00 per share following the underwriters' exercise of their option to purchase additional shares. Net proceeds, after deducting underwriting commissions and offering costs paid by the Company, were $64.5 million.

The Company will continue to seek funds through equity or debt financings, collaborative or other arrangements with corporate sources, or through other sources of financing, but there is no assurance that such financing will be available at terms acceptable to the Company, if at all.

Reverse Stock Split

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 1-for-14.5 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 stock split. All issued and outstanding common stock, options to purchase common stock and per share amounts contained in the consolidated financial statements have been retroactively adjusted to reflect the reverse stock split for all periods presented.

Note 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 Limited and have been prepared in conformity with accounting principles generally accepted in the United States of America ("GAAP"). All intercompany balances and transactions have been eliminated in consolidation.

The financial statements of Protagonist Pty Limited 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, 2017 and 2016 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.

Foreign currency translation gains and losses are reported as a component of stockholders' equity in accumulated other comprehensive loss on the consolidated balance sheets.

Use of Estimates

The preparation of the consolidated financial statements in conformity with GAAP requires management to make estimates, assumptions and judgments 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 reported amounts of revenues and expenses during the reporting period. On an ongoing basis, management evaluates its estimates, including those related to revenue, recognition, 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 forecasted amounts and future events. Actual results may differ significantly 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 of the Company's cash is held by three financial institutions that management believes are of high credit quality. Such deposits may, at times, exceed federally insured limits. The primary focus of the Company's investment strategy is to preserve capital and to meet liquidity requirements. The Company's cash equivalents and available-for-sale securities are managed by external managers within the guidelines of the Company's investment policy. The Company's investment policy addresses the level of credit exposure by limiting concentration in any one corporate issuer and establishing a minimum allowable credit rating. To manage its credit risk exposure, the Company maintains its portfolio of cash equivalents and available-for-sale securities in fixed income securities denominated and payable in U.S. dollars. Permissible investments of fixed income securities include obligations of the United States government and its agencies, money market instruments including commercial paper

and negotiable certificates of deposit, and highly rated corporate debt obligations and money market funds. The Company has not experienced any material credit losses on its investments.

Cash Equivalents

Cash equivalents that are readily convertible to cash are stated at cost, which approximates fair value. The Company considers all highly liquid investments purchased with an original maturity of three months or less to be cash equivalents.

Restricted Cash

Restricted cash consists of cash balances primarily held as security in connection with the Company's corporate credit card and a letter of credit related to the Company's facility lease entered into in March 2017.

Cash as Reported in Consolidated Statements of Cash Flows

Cash as reported in the consolidated statements of cash flows includes the aggregate amounts of cash and cash equivalents and the restricted cash as presented on the consolidated balance sheets.

Cash as reported in the consolidated statements of cash flows consists of (in thousands):

	December 31,		
	2017	2016	2015
Cash and cash equivalents	$ 106,029	$ 21,084	$ 4,055
Restricted cash - current	10	10	10
Restricted cash - noncurrent	450	—	—
Cash balance in consolidated statements of cash flows	$ 106,489	$ 21,094	$ 4,065

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.

Fair Value of Financial Instruments

Fair value accounting is applied to 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 equivalents, receivable from collaboration partner, accounts payable and accrued expenses and other payables approximate fair value due to their short-term maturities. See Note 4. Fair Value Measurements regarding the fair value of the Company's other financial assets and liabilities.

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 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.

Comprehensive Loss

Comprehensive loss includes net loss as well as other changes in stockholders' equity (deficit) that result from transactions and economic events other than those from 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 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% likelihood 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 unrecognized tax benefits.

Revenue Recognition

Effective July 1, 2017, the Company adopted Accounting Standards Codification Topic 606, *Revenue from Contracts with Customers* ("ASC 606") using the full retrospective transition method. The Company did not have any effective contracts within the scope of this guidance prior to July 1, 2017. Accordingly, the Company did not elect to use any of the practical expedients permitted related to adoption, and the adoption of ASC 606 had no impact on the Company's financial position, results of operations or liquidity. This standard applies to all contracts with customers, except for contracts that are within the scope of other standards, such as leases, insurance, collaboration arrangements and financial instruments. Under ASC 606, the Company recognizes revenue when its customer obtains control of promised goods or services, in an amount that reflects the consideration which the Company expects to receive in exchange for those goods or services. To determine revenue recognition for arrangements that the Company determines are within the scope of ASC 606, the Company performs the following five steps: (i) identify the contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue when (or as) the Company satisfies a performance obligation. The Company only applies the five-step model to contracts when it is probable that Company will collect the consideration it is entitled to in exchange for the goods or services it transfers to the customer. At contract inception, once the contract is determined to be within the scope of ASC 606, the Company assesses the goods or services promised within each contract and determines those that are performance obligations and assesses

whether each promised good or service is distinct. The Company then recognizes as revenue the amount of the transaction price that is allocated to the respective performance obligation when (or as) the performance obligation is satisfied.

The Company entered into a license and collaboration agreement that became effective upon the resolution of regulatory requirements during the third quarter of 2017 which is within the scope of ASC 606, under which it has licensed certain rights to its PTG-200 product candidate to a third party, and may enter into other such arrangements in the future. The terms of the arrangement include payment to the Company of one or more of the following: non-refundable, up-front license fees, development and regulatory and commercial milestone payments, and royalties on net sales of licensed products.

Licenses of intellectual property: If the license to the Company's intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, the Company recognizes revenue from non-refundable, up-front fees allocated to the license when the license is transferred to the customer and the customer is able to use and benefit from the license. For licenses that are bundled with other promises, the Company utilizes judgement to assess the nature of the combined performance obligation to determine whether the combined performance obligation is satisfied over time or at a point in time and, if over time, the appropriate method of measuring proportional performance for purposes of recognizing revenue from non-refundable, up-front fees. The Company evaluates the measure of proportional performance each reporting period and, if necessary, adjusts the measure of performance and related revenue recognition.

Milestone payments: At the inception of each arrangement that includes development, regulatory or commercial milestone payments, the Company evaluates whether the milestones are considered probable of being reached and estimates the amount to be included in the transaction price. ASC 606 suggests two alternatives to use when estimating the amount of variable consideration: the expected value method and the most likely amount method. Under the expected value method, an entity considers the sum of probability-weighted amounts in a range of possible consideration amounts. Under the most likely amount method, an entity considers the single most likely amount in a range of possible consideration amounts. Whichever method is used, it should be consistently applied throughout the life of the contract; however, it is not necessary for the Company to use the same approach for all contracts. The Company expects to use the most likely amount method for development and regulatory milestone payments. If it is probable that a significant revenue reversal would not occur, the associated milestone value is included in the transaction price. Milestone payments that are not within the control of the Company or the licensee, such as regulatory approvals, are not considered probable of being achieved until those approvals are received. The transaction price is then allocated to each performance obligation on a relative stand-alone selling price basis. The Company recognizes revenue as or when the performance obligations under the contract are satisfied. At the end of each subsequent reporting period, the Company re-evaluates the probability or achievement of each such milestone and any related constraint, and if necessary, adjusts its estimates of the overall transaction price. Any such adjustments are recorded on a cumulative catch-up basis, which would affect revenues and earnings in the period of adjustment. To date, the Company has not recognized any milestone payments resulting from its collaboration arrangement.

Royalties: For arrangements that include sales-based royalties, including milestone payments based on the level of sales, and the license is deemed to be the predominant item to which the royalties relate, the Company recognizes revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). To date, the Company has not recognized any royalty revenue resulting from its collaboration arrangement.

Up-front payments and fees are recorded as deferred revenue upon receipt or when due, and may require deferral of revenue recognition to a future period until the Company performs its obligations under these arrangements. Amounts payable to the Company are recorded as accounts receivable when the Company's right to consideration is unconditional. The Company does not assess whether a contract has a significant financing component if the expectation at contract inception is such that the period between payment by the customer and the transfer of the promised goods or services to the customer will be one year or less.

Research and Development Costs

Research and development costs are expensed as incurred, unless there is an alternate future use in other research and development projects. Research and development costs include salaries and benefits, stock-based compensation expense, laboratory supplies and facility-related overhead, outside contracted services including clinical trial costs, manufacturing and process development costs for both clinical and preclinical materials, research costs, development milestone payments under license and collaboration agreements, and other consulting services.

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 services provided but not yet invoiced and includes these costs in accrued expenses and other payables 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 at each balance sheet date. As actual costs become known, the Company adjusts its accrued liabilities. The Company has not experienced any material differences between accrued liabilities and actual costs incurred. However, the status and timing of actual services performed, number of patients enrolled, and the rate of patient enrollment 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 Tax Incentive

The Company is eligible under the AusIndustry research and 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 annual turnover of less than AUD 20.0 million and cannot be controlled by income tax exempt entities. The research and development tax incentive is recognized as a reduction to 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.

Under certain conditions, research and development activities conducted outside Australia ("overseas finding") also qualify for the research and development tax incentive. Funds received for overseas finding are at a risk of clawback until substantiation that less than 50% of 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 expenses is not recognized until the Company can substantiate that more than 50% of the total project expenditure will occur in Australia.

When there is reasonable assurance that the grant will be received with remote risk of clawback, the relevant expenditure has been incurred, and the consideration can be reliably measured, the Company records the research and development incentive, including the overseas finding funds, as research and development tax incentive receivable and a reduction of research and development expenses to reflect that the funds are owed to the Company for the period the eligible costs are incurred.

SBIR Grants

The Company has been awarded Small Business Innovation Research ("SBIR") grants from the National Institute of Diabetes and Digestive and Kidney Diseases ("NIDDK") and the National Heart, Lungs and Blood Institute ("NHLBI") of the National Institutes of Health ("NIH") in support of its research activities. The Company records the eligible costs incurred under the SBIR grants as a reduction of research and development expenses.

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. At the time of the exercise or expiration of the option, the fair 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 continued to adjust the warrant liability for changes in fair value until the earlier of the exercise of the warrants or expiration on May 10, 2016, 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 and is based on the value of the portion of stock-based payment awards that is ultimately expected to vest. The Company adopted Accounting Standards Update ("ASU") No. 2016-09, *Compensation-Stock Compensation (Topic 718): Improvements to Employee Share-Based Payment Accounting* effective January 1, 2017 and has elected to recognize forfeitures of share-based payment awards as they occur on a prospective basis. Prior to January 1, 2017, the Company's stock-based compensation was reduced for the estimated forfeitures at the date of grant and revised, if necessary, in subsequent periods if actual forfeitures differed 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, if applicable. 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 is anti-dilutive given the net loss of the Company.

Recently Adopted Accounting Pronouncements

In May 2014, the Financial Accounting Standards Board ("FASB") issued ASU No. 2014-09, which amends the guidance for accounting for revenue from contracts with customers. This ASU supersedes the revenue recognition requirements in ASC Topic 605, *Revenue Recognition*, and creates a new ASC Topic 606, *Revenue from Contracts with Customers*. Subsequent to May 2014, the FASB issued additional guidance that delayed the effective date and clarified various aspects of the new guidance, including principal versus agent considerations, identifying performance obligations and licensing, and also included other improvements and practical expedients. The Company adopted this new guidance effective July 1, 2017 using the full retrospective transition method. The Company did not have any effective contracts within the scope of this guidance prior to July 1, 2017. Accordingly, the Company did not elect to use

any of the practical expedients permitted under the transition guidance, and the adoption had no impact on the Company's previously reported financial position, results of operations or liquidity.

In November 2015, the 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 income taxes are classified on the balance sheet. This guidance 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, and early adoption is permitted. The Company adopted this guidance effective January 1, 2017. The adoption of this guidance did not have a material impact on the Company's financial position, results of operations or liquidity.

In March 2016, the FASB issued ASU No. 2016-09, *Compensation-Stock Compensation (Topic 718): Improvements to Employee Share-Based Payment Accounting*, which is intended to simplify several aspects of accounting for employee share-based payment transactions, including 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 guidance is effective for fiscal years and interim periods within those years beginning after December 15, 2016, and early adoption is permitted. The Company adopted this guidance effective January 1, 2017 and has elected to recognize forfeitures of share-based payment awards as they occur on a prospective basis. The impact of the adoption of ASU No. 2016-09 was not material to the Company's consolidated financial statements. The adoption of this guidance did not have a material impact on the income tax effects of share-based payment awards as the resulting change in the Company's deferred income tax assets is fully offset by a corresponding deferred income tax asset valuation allowance.

In November 2016, the FASB issued ASU No. 2016-18, *Statement of Cash Flows (Topic 230): Restricted Cash,* which requires the presentation of changes in restricted cash or restricted cash equivalents on the statement of cash flows. This guidance is effective for the fiscal years and interim periods within those years beginning after December 15, 2017, with early adoption permitted. The Company early adopted this guidance effective March 31, 2017, and, accordingly, restricted cash amounts are included with cash and cash equivalents when reconciling the beginning-of-period and end-of-period total amounts of cash reflected on the accompanying consolidated statements of cash flows. The Company has adopted ASU No. 2016-18 retrospectively and has revised the prior period cash flows from investing activities, beginning cash balance, and ending cash balance to reflect the change in presentation of restricted cash. Other than the change in presentation in the accompanying consolidated statements of cash flows, the adoption of this guidance had no effect on the Company's financial position, results of operations or liquidity.

Recently Issued Accounting Pronouncements Not Adopted as of December 31, 2017

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. This guidance is effective for fiscal years beginning after December 15, 2018, including interim periods within those fiscal years. Early adoption is permitted. Lessees (for capital and operating leases) are required to apply the modified retrospective transition method for leases existing at, or entered into after, the beginning of the earliest comparative period presented in the financial statements. The modified retrospective method does not require any transition accounting for leases that did not exist before the earliest comparative period presented. The Company established a cross-functional implementation team to review current lease accounting policies and practices and assess the impact of this guidance on the Company's consolidated financial statements and disclosures. While the Company is currently reviewing its lease portfolio and evaluating and interpreting the requirements under the new guidance, including available accounting policy elections, it expects that its non-cancellable operating lease commitments will be subject to the new guidance and recognized as right-of-use assets and operating lease liabilities on the Company's consolidated balance sheets, and that the adoption of this new guidance will not have a material impact on its results of operations or liquidity.

In June 2016, the FASB issued ASU No. 2016-13, *Financial Instruments - Credit Losses (Topic 326)*, which is intended to provide financial statement users with more useful information about expected credit losses on financial

assets held by a reporting entity at each reporting date. The new standard replaces the existing incurred loss impairment methodology with a methodology that requires consideration of a broader range of reasonable and supportable forward-looking information to estimate all expected credit losses. This guidance is effective for fiscal years and interim periods within those years beginning after December 15, 2019, and early adoption is permitted for fiscal years and interim periods within those years beginning after December 15, 2018. The Company is currently evaluating the impact of this new guidance on its consolidated financial statements and disclosures.

In August 2016, the FASB issued ASU No. 2016-15, *Statement of Cash Flows (Topic 230): Classification of Certain Cash Receipts and Cash Payments,* which clarifies the classification of certain cash receipts and cash payments in the statements of cash flow to eliminate the diversity in practice related to eight specific cash flow issues. This guidance is effective for fiscal years and interim periods within those years beginning after December 15, 2017, and early adoption is permitted. The Company expects that the adoption of this new guidance will not have a material impact on its consolidated financial statements and disclosures.

In May 2017, the FASB issued ASU No. 2017-09, *Compensation - Stock Compensation (Topic 718): Scope of Modification Accounting*, which provides guidance on the types of changes to the terms and conditions of share-based payment awards to which an entity would be required to apply modification accounting. Specifically, an entity would not apply modification accounting if the fair value, vesting conditions and classification of the awards are the same immediately before and after the modification. This guidance is effective for fiscal years and interim periods within those years beginning after December 15, 2017, and early adoption is permitted. The Company expects that the adoption of this new guidance will not have a material impact its consolidated financial statements and disclosures.

Note 3. Janssen License and Collaboration Agreement

Agreement Terms

On May 26, 2017, the Company and Janssen Biotech, Inc., ("Janssen"), one of the Janssen Pharmaceutical Companies of Johnson & Johnson, entered into an exclusive license and collaboration agreement for the development, manufacture and commercialization of PTG-200 worldwide for the treatment of Crohn's disease ("CD") and ulcerative colitis ("UC"). Janssen is a related party to the Company as Johnson & Johnson Innovation - JJDC, Inc., a significant shareholder of the Company, and Janssen are both subsidiaries of Johnson and Johnson. PTG-200 is the Company's oral Interleukin 23 receptor ("IL-23R") antagonist drug candidate currently in development. The Janssen License and Collaboration Agreement became effective on July 13, 2017. Upon the effectiveness of the agreement, the Company became eligible for and received a non-refundable, upfront cash payment of $50.0 million from Janssen.

Under the Janssen License and Collaboration Agreement, the Company granted to Janssen an exclusive worldwide license to develop, manufacture and commercialize PTG-200 and related IL-23R compounds for all indications, including CD and UC. The Company is responsible, at its own expense, for the conduct of the Phase 1 clinical trial for PTG-200, and Janssen will be responsible for the conduct of a potential Phase 2 clinical trial for PTG-200 in CD, including filing the Phase 2 Investigational New Drug ("IND") application. All such clinical trials will be conducted in accordance with a mutually agreed upon clinical development plan and budget. Development costs for the Phase 2 clinical trial will be shared between the parties on an 80%/20% basis, with Janssen assuming the larger share. Should Janssen elect to retain its license following completion of the Phase 2 clinical trial, it will be responsible, at its own expense, for the manufacture, continued development of, seeking regulatory approval for, and commercialization of PTG-200 worldwide. The parties' development activities under the Janssen License and Collaboration Agreement through the Phase 2 clinical trial will be overseen by a joint governance structure which will have equal representation by both parties unless both parties mutually agree to disband such structure or the Company has provided written notice to Janssen of its intention to disband and no longer participate in such structure.

The Company is eligible to receive a $25.0 million payment upon filing of the Phase 2 IND. Following the conclusion of the planned Phase 2a portion of the Phase 2 clinical trial, if Janssen elects to maintain its license rights and continue the development of PTG-200 in the Phase 2b portion of such clinical trial (the "First Opt-in Election"), the Company would be eligible to receive a $125.0 million payment. Following the conclusion of the planned Phase 2b portion of the Phase 2 clinical trial, if Janssen elects again to maintain its license rights (the "Second Opt-in Election"),

the Company would be eligible to receive a $200.0 million payment. In addition to the opt-in fees, the Company is eligible to receive additional potential development, regulatory and sales milestone payments of up to an aggregate of $590.0 million, and tiered royalties paid as a percentage of Janssen's worldwide net sales at rates ranging from ten to the mid-teens, with certain customary reductions under certain circumstances. If Janssen does not make either the First Opt-in Election or the Second Opt-in Election, the Janssen License and Collaboration Agreement will terminate. If Janssen does not make the Second Opt-in Election, or if at any time after the Second Opt-in Election, Janssen terminates the Janssen License and Collaboration Agreement, the Company would be obligated to pay Janssen a low single-digit royalty on worldwide net sales of PTG-200. The Company would also have an option to provide up to 30% of the required U.S. details for PTG-200 to prescribers, using its own sales force personnel, upon commercial launch in the United States. If such right is exercised by the Company, the Company's detailing costs would be reimbursed by Janssen at a mutually agreed cost per primary detailing equivalent.

The Janssen License and Collaboration Agreement contains customary representations, warranties and covenants by the Company and Janssen and includes an obligation by the Company not to develop or commercialize other compounds which also target IL-23R outside of the Janssen License and Collaboration Agreement until completion of the Phase 2b portion of the Phase 2 clinical trial. Each of the Company and Janssen is required to indemnify the other party against all losses and expenses related to breaches of its representations, warranties and covenants under the Janssen License and Collaboration Agreement.

The Janssen License and Collaboration Agreement remains in effect until the royalty obligations cease following patent and regulatory expiry, unless terminated earlier. Either the Company or Janssen may terminate the Janssen License and Collaboration Agreement for uncured material breach. Janssen retains the right to terminate the Janssen License and Collaboration Agreement for convenience and without cause on written notice of a certain period to the Company. Upon a termination of the Janssen License and Collaboration Agreement, all rights revert back to the Company, and in certain circumstances, if such termination occurs during ongoing clinical trials, Janssen would, if requested, provide certain financial and operational support to the Company for the completion of such trials.

Revenue Recognition

The Company identified the following material promises under the Janssen License and Collaboration Agreement: (1) the license related to PTG-200, (2) the performance of development services, including regulatory support, during the Phase 1 clinical trial for PTG-200 through the filing of the IND by Janssen, and (3) compound supply services for Phase 1 and Phase 2 activities. The Company considered that the license has standalone functionality and is capable of being distinct. However, the Company determined that the license is not distinct from the development and compound supply services within the context of the agreement because the development and compound supply services significantly increase the utility of the intellectual property.

Specifically, the Company's development, manufacturing and commercialization license can only provide benefit to Janssen in combination with the Company's development services in the Phase 1 study. The intellectual property ("IP") related to the peptide technology platform, which is proprietary to the Company, is the foundation for the development activities related to the treatment for CD. The compound supply services are a necessary and integral part of the development services as they could only be conducted utilizing the outcomes of these services. Given the development services under the Janssen Collaboration Agreement are expected to involve significant further development of the initial IP, the Company has concluded that the development and compound supply services are not distinct from the license, and thus the license, development services and compound supply services are combined into a single performance obligation. The nature of the combined performance obligation is to provide development and compound supply services to Janssen under the arrangement.

The Company also evaluated whether the fees related to the First Opt-in Election and Second Opt-in Election are options with material rights. These two options include additional sublicense rights and patent rights transferred to Janssen upon exercising both of these options. The Company concluded that Janssen's opt in rights are not options with material rights because the $50.0 million upfront payment to the Company was not negotiated to provide incremental discount for the future opt in payments at the end of Phase 2a and Phase 2b. The option to "opt in" provides Janssen with a license for IP that has been improved from the license initially granted for a term in the case of the opt in after

completion of Phase 2a and then a perpetual license in the case of opt in after completion of Phase 2b. Therefore, the First Opt-in Election and Second Opt-in Election options are not considered to be material rights. The option fees will be recognized as revenue when, and if, Janssen exercises its options because the Company has no further performance obligations at that point.

For revenue recognition purposes, the Company determined that the duration of the contract begins on the effective date of July 13, 2017 and ends upon completion of Phase 2a activities. The contract duration is defined as the period in which parties to the contract have present enforceable rights and obligations. The Company analyzed the impact of Janssen terminating the agreement prior to the completion of Phase 2a and determined that there were significant economic penalties to Janssen for doing so. The Company believes that if Janssen terminates the agreement upon completion of Phase 2a, the forfeiture of the remaining license rights and payment of 50% of the remaining Phase 2 costs is not a significant economic penalty when compared to paying $125.0 million as an opt in license fee to continue the use of the License. Thus, the duration of the contract is limited to the end of Phase 2a.

The Company determined that the transaction price of the Janssen License and Collaboration Agreement was $53.9 million as of December 31, 2017, a decrease of $0.4 million from the transaction price of $54.3 million as of September 30, 2017. In order to determine the transaction price, the Company evaluated all the payments to be received during the duration of the contract. The Company determined that the $50.0 million upfront payment, the $25.0 million payment payable upon filing of the Phase 2 IND, which is fully constrained as of December 31, 2017, and $3.9 million of estimated variable consideration for cost-sharing payments from Janssen for agreed upon services related to Phase 2 activities constituted consideration to be included in the transaction price, which is to be allocated to the combined performance obligation. The decrease in transaction price from September 30, 2017 was due to a decrease in variable consideration related to compound supply services. The Company will re-evaluate the transaction price in each reporting period and as uncertain events are resolved or other changes in circumstances occur.

As part of the evaluation for determining that the $25.0 million payment upon filing of the Phase 2 IND is fully constrained as of December 31, 2017, the Company considered several factors, including the stage of development of PTG-200 and that achievement of the milestone is outside of the Company's control, and concluded that the filing of the Phase 2 IND is not probable at this time. If and when the filing of the Phase 2 IND becomes probable, the $25.0 million payment will be constrained by contra revenue amounts for payments that the Company expects to make for 20% of the cost of Phase 2 activities to be performed by Janssen. The additional potential development, regulatory and sales milestone payments of up to an aggregate of $590.0 million after the completion of Phase 2a activities that the Company is eligible to receive are outside the contract term and as such have been excluded from the transaction price. Any consideration related to sales-based milestones (including royalties) will be recognized when the related sales occur as they were determined to relate predominantly to the license granted to Janssen and therefore have also been excluded from the transaction price. At the end of each reporting period, the Company will update its assessment of whether an estimate of variable consideration is constrained and update the estimated transaction price accordingly.

Variable consideration for cost-sharing payments related to agreed upon services for Phase 2 activities that the Company performs within the duration of the contract are included in the transaction price at an amount equal to 80% of the estimated budgeted costs for these activities, including primarily internal full-time equivalent effort and third party contract costs. The Company is responsible for 20% of the development costs for the Phase 2 clinical trial. Accordingly, a significant portion of this work is expected to be performed by Janssen. Because the Phase 2 clinical trial activity is related to the license, it is not capable of being distinct. This is because both the Company and Janssen cannot benefit from these activities absent the Phase 1 activities. As the Phase 2 activities for which the Company will share 20% of the cost activities are not capable of being distinct and are not separately identifiable within the context of the contract, they are not a distinct service that Janssen transfers to the Company. Therefore, the consideration payable to Janssen is accounted for as a reduction in the transaction price. The Company and Janssen make quarterly cost-sharing payments to one another in amounts necessary to ensure that each party bears its contractual share of the overall shared costs incurred. The Company accounts for cost-sharing payments from Janssen as increases in license and collaboration revenue in its consolidated statements of operations, while cost-sharing payments to Janssen are accounted for as reductions in license and collaboration revenue, or contra-revenue. Costs incurred by the Company related to agreed upon services for Phase 2 activities under the Janssen License and Collaboration Agreement are recorded as research and development expenses in its consolidated statements of operations.

In summary, the license, the development activities for Phase 1 activities and the agreed upon services for Phase 2 activities are combined as one performance obligation that will be performed over the duration of the contract, which is from the effective date of the Janssen License and Collaboration Agreement through to the completion of Phase 2a activities. Since the Company has determined that the combined performance obligation is satisfied over time, ASC 606 requires the Company to select a single revenue recognition method for the performance obligation that faithfully depicts the Company's performance in transferring control of the services. The guidance allows entities to choose between two methods to measure progress toward complete satisfaction of a performance obligation:

1. Output methods - recognize revenue on the basis of direct measurements of the value to the customer of the goods or services transferred to date relative to the remaining goods or services promised under the contract (e.g. surveys of performance completed to date, appraisals of results achieved, milestones reached, time elapsed, and units of produced or units delivered); and

2. Input methods - recognize revenue on the basis of the entity's efforts or inputs to the satisfaction of a performance obligation (e.g., resources consumed, labor hours expended, costs incurred, or time elapsed) relative to the total expected inputs to the satisfaction of that performance obligation.

The Company concluded that it will utilize a cost-based input method to measure proportional performance and to calculate the corresponding amount of revenue to recognize. The Company believes this is the best measure of progress because other measures do not reflect how the Company transfers its performance obligation to Janssen. In applying the cost-based input methods of revenue recognition, the Company uses actual costs incurred relative to budgeted costs to fulfill the combined performance obligation. These costs consist primarily of internal full-time equivalent effort and third-party contract costs. Revenue will be recognized based on actual costs incurred as a percentage of total budgeted costs as the Company completes its performance obligations, which the Company believes will be fulfilled within the next 12 months. A cost-based input method of revenue recognition requires management to make estimates of costs to complete the Company's performance obligations. In making such estimates, significant judgment is required to evaluate assumptions related to cost estimates. The cumulative effect of revisions to estimated costs to complete the Company's performance obligations will be recorded in the period in which changes are identified and amounts can be reasonably estimated. A significant change in these assumptions and estimates could have a material impact on the timing and amount of revenue recognized in future periods.

For the year ended December 31, 2017, the Company recognized $20.1 million of license and collaboration revenue. This amount included $19.0 million of the transaction price for the Janssen License and Collaboration Agreement recognized based on proportional performance, and $1.1 million for other services related to Phase 2 activities performed by the Company on behalf of Janssen that are not included in the performance obligations identified under the Janssen License and Collaboration Agreement.

The following table presents changes in the Company's contract assets and liabilities for the year ended December 31, 2017 (in thousands):

Year ended December 31, 2017	Balance at Beginning of Period	Additions	Deductions	Balance at End of Period
Contract assets:				
Receivable from collaboration partner - related party	$ —	$ 51,816	$ (50,000)	$ 1,816
Contract liabilities:				
Deferred revenue - related party	$ —	$ 50,708	$ (18,956)	$ 31,752

Deferred revenue related to the Janssen License and Collaboration Agreement of $31.8 million as of December 31, 2017, which was comprised of the $50.0 million upfront payment and $0.7 million of cost sharing payments from Janssen for agreed upon services for Phase 2 activities, less $19.0 million of license and collaboration revenue recognized from the effective date of the contract, will be recognized as the combined performance obligation is satisfied. The Company also recorded a $1.8 million receivable from collaboration partner as of December 31, 2017 for cost sharing amounts payable from Janssen.

During the year ended December 31, 2017, the Company did not recognize any revenue from amounts included in the contract asset and the contract liability balances at the beginning of the period or from performance obligations satisfied in previous periods. None of the costs to obtain or fulfill the contract were capitalized.

Note 4. 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 quotations, or valuation techniques that maximize the use of observable inputs and minimize the use of unobservable inputs to the extent possible and considers counterparty credit risk in its assessment of fair value.

The following table presents the fair value of the Company's financial assets determined using the inputs defined above (in thousands).

	December 31, 2017			
	Level 1	Level 2	Level 3	Total
Assets:				
Money market funds	$ 48,704	$ —	$ —	$ 48,704
Corporate bonds	—	6,247	—	6,247
Commercial paper	—	58,524	—	58,524
Governmental bonds	—	40,303	—	40,303
Total financial assets	$ 48,704	$ 105,074	$ —	$ 153,778

	December 31, 2016			
	Level 1	Level 2	Level 3	Total
Assets:				
Money market funds	$ 11,270	$ —	$ —	$ 11,270
Corporate bonds	—	21,841	—	21,841
Commercial paper	—	10,769	—	10,769
Governmental bonds	—	41,289	—	41,289
Total financial assets	$ 11,270	$ 73,899	$ —	$ 85,169

The Company's corporate bonds, commercial paper and government bonds 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.

Note 5. 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, 2017			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Money market funds	$ 48,704	$ —	$ —	$ 48,704
Corporate bonds	6,254	—	(7)	6,247
Commercial paper	58,524	—	—	58,524
Government bonds	40,428	—	(125)	40,303
Total cash equivalents and available-for-sale securities	$ 153,910	$ —	$ (132)	$ 153,778
Classified as:				
Cash equivalents				$ 104,348
Available-for-sale securities - current				37,972
Available-for-sale securities - noncurrent				11,458
Total cash equivalents and available-for-sale securities				$ 153,778

	December 31, 2016			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Money market funds	$ 11,270	$ —	$ —	$ 11,270
Corporate bonds	21,886	—	(45)	21,841
Commercial paper	10,769	—	—	10,769
Government bonds	41,316	2	(29)	41,289
Total cash equivalents and available-for-sale securities	$ 85,241	$ 2	$ (74)	$ 85,169
Classified as:				
Cash equivalents				$ 18,504
Available-for-sale securities - current				56,515
Available-for-sale securities - noncurrent				10,150
Total cash equivalents and available-for-sale securities				$ 85,169

All available-for-sale securities - current held as of December 31, 2017 and 2016 had contractual maturities of less than one year. All available securities - noncurrent held as of December 31, 2017 and 2016 had contractual maturities of at least one year but less than two years. There were no material realized gains or realized 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,	
	2017	2016
Prepaid clinical and research related expenses	$ 2,324	$ 2,488
Prepaid insurance	378	408
Other	1,071	498
Prepaid expenses and other current assets	$ 3,773	$ 3,394

Property and Equipment, Net

Property and equipment, net consisted of the following (in thousands):

	December 31,	
	2017	2016
Laboratory equipment	$ 2,177	$ 1,650
Furniture and computer equipment	270	163
Leasehold improvements	26	62
Total property and equipment	2,473	1,875
Less: accumulated depreciation and amortization	(1,594)	(1,313)
Property and equipment, net	$ 879	$ 562

Depreciation expense for the years ended December 31, 2017, 2016, and 2015 was $406,000, $317,000, and $247,000, respectively. As of December 31, 2017 and 2016, $1,200 and $8,000, respectively, of property and equipment, net, was located in Australia. The remainder of the Company's property and equipment is located in the United States.

Accrued Expenses and Other Payables

Accrued expenses and other payables consisted of the following (in thousands):

	December 31,	
	2017	2016
Accrued clinical and research related expenses	$ 6,437	$ 3,617
Accrued employee related expenses	2,718	1,420
Accrued professional service fees	267	115
Other	124	120
Accrued expenses and other payables	$ 9,546	$ 5,272

Note 6. 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 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 acquired by the Company. The nomination of PTG-300 as a development candidate triggered a $250,000 payment from the Company to the former collaboration partner. The initiation of a Phase 1 clinical trial for PTG-300 triggered an additional $250,000 payment from the Company to the former collaboration partner. The Company has the right, but not the obligation, to further develop and commercialize the product 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 or the expiration of the last patent covering the product. For each of the years ended December 31, 2017 and 2016, the Company recorded research and development expense of $250,000 under this agreement. There were no such costs incurred for the year ended December 31, 2015.

Note 7. Government Programs

Research and Development Tax Incentive

The Company recognized AUD 1.7 million ($1.3 million), AUD 5.3 million ($4.0 million) and AUD 978,000 ($736,000) as a reduction of research and development expenses for the years ended December 31, 2017, 2016 and

2015, respectively, in connection with the research and development tax incentive from Australia. As of December 31, 2017 and 2016, the research and development tax incentive receivable was AUD 1.7 million ($1.3 million) and AUD 3.1 million ($2.2 million), respectively.

In March 2016, the Company received AUD 237,000 ($182,000) for overseas findings and recorded the funds as deferred tax incentive in accrued expenses and other payables on the consolidated balance sheet due to the possibility that the funds could have to be repaid. In December 2016, the Company's research and development project under the AusIndustry research and development tax incentive program was complete and the Company substantiated that more than 50% of the total project expenditures occurred in Australia. Therefore, the overseas finding related incentive amounts were no longer deemed to be at risk of clawback and the Company recognized such amounts in December 2016 as a reduction of research and development expenses for the overseas findings received in 2016.

Based on the nature of the amounts received under the Janssen License and Collaboration Agreement, the Company has concluded that these amounts should be classified as statutory income for Australian taxation purposes. Accordingly, they should not be included in the calculation of annual turnover for the purposes of determining eligibility for the refundable research and development tax offset.

SBIR Grant

In May 2017, the Company was awarded a Phase 2 SBIR Grant from the NIDDK of the NIH in support of research aimed at developing biomarkers that define IL-23R target engagement by oral peptide antagonists and the effects of that engagement of downstream signaling. The total grant award was $1.3 million and is for the period from May 2017 to April 2019.

In July 2016, the Company was awarded a Phase 1 SBIR Grant from the NHLBI of the NIH in support of preclinical research aimed at discovering and optimizing lead molecules as novel peptide mimetics of the hepcidin hormone. The total grant award was $219,000 and was for the period from August 2016 to January 2017.

In September 2015, the Company was awarded a Phase 1 SBIR Grant from the NIDDK of the NIH in support of research on orally stable peptide antagonists of IL-23R as potential treatments for IBD. The total grant award was $224,000 and was for the period from September 2015 to August 2016.

The Company recognizes a reduction to research and development expenses when expenses related to the grants have been incurred and the grant funds become contractually due from NIH. The Company recorded $182,000, $169,000 and $155,000 as a reduction of research and development expenses for the years ended December 31, 2017, 2016 and 2015, respectively. The Company recorded a receivable for $58,000 and $100,000 as of December 31, 2017 and 2016, respectively, to reflect the eligible costs incurred under the grants that are contractually due to the Company, and such amounts are included in prepaid expenses and other current assets on the consolidated balance sheets.

Note 8. Commitments and Contingencies

Lease Arrangements

In March 2017, the Company entered into a lease agreement for office and laboratory space located in Newark, California. The Company relocated its operations to the new facility in May 2017. The Company provided the landlord with a $450,000 letter of credit collateralized by restricted cash as security deposit for the lease, which expires in May 2024. The Company is entitled to tenant improvement allowances of approximately $469,000, any unused portion of which expires in December 2018. The Company records tenant improvement allowances as deferred rent when funds are received and associated capital expenditures as leasehold improvements that will be amortized over the shorter of their useful life or the remaining term of the lease.

The following table summarizes the Company's future minimum lease payments related to the Newark facility as of December 31, 2017 (in thousands):

Year Ending December 31:	Amount
2018	$ 1,667
2019	1,941
2020	2,000
2021	2,060
2022	2,121
Thereafter	3,106
Total	$ 12,895

The Company's rent expense was $1.4 million, $408,000 and $280,000 million for the years ended December 31, 2017, 2016 and 2015, respectively. Rent expense is recognized on a straight-line basis over the term of the lease 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 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.

Note 9. 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 would become exercisable only when certain milestones were met on programs begun as a result of collaborations entered into in 2011 and 2012. In particular, 50% of the warrants would become exercisable upon the Company publicly announcing its first IND candidate to the extent such IND candidate was the result of, or related to, the Company's previous collaboration(s) with Ironwood Pharmaceuticals and/or Zealand Pharma A/S, and the balance would become exercisable upon the first dosing of a human patient in a clinical trial that was the 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 the first tranche and second tranche, respectively.

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. Immediately prior to the

exercise of the warrants, the fair value of the warrants 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 probability-weighted expected return method ("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 exercise of warrants, the redeemable convertible preferred stock warrant liability of $1.0 million was reclassified to redeemable convertible preferred stock.

In May 2016, the remaining warrants for the purchase of 2,000,000 shares of Series B redeemable convertible preferred stock expired unexercised.

The Company recorded a charge of $525,000 for the year ended December 31, 2016, representing the increase in the fair value of the redeemable convertible preferred stock warrant liability in the consolidated statements of operations. The Company recorded a gain of $543,000 for the year ended December 31, 2015, representing the decrease in the fair value of the redeemable convertible preferred stock warrant liability in the consolidated statements of operations. There were no such charges incurred for the year ended December 31, 2017.

Note 10. Redeemable Convertible Preferred Stock

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.

Following the closing of the IPO, all outstanding shares of the redeemable convertible preferred stock converted into 8,577,571 shares of common stock and the related carrying value was reclassified to common stock and additional paid-in capital. There were no shares of redeemable convertible preferred stock outstanding as of December 31, 2016 or 2017.

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

As only the passage of time was required for Series A, B and C to become redeemable, the Company was accreting 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) up to the IPO date. In the event of a change of control of the Company, proceeds would 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 had converted their redeemable convertible preferred stock into shares of common stock. Therefore, redeemable convertible preferred stock was classified outside of stockholders' equity (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 were not solely within the Company's control.

The Company recorded $558,000 and $75,000 for the accretion of the redeemable convertible preferred stock during the years ended December 31, 2016 and 2015, respectively. 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. There were no such charges incurred for the year ended December 31, 2017.

Note 11. Redeemable Convertible Preferred Stock Tranche Liability

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.

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 tranche 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 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 tranche 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 years, 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 tranche liability was terminated and the balance of the liability of $5.8 million was reclassified to redeemable convertible preferred stock.

For the years ended December 31, 2016 and 2015, the Company recorded a charge of $4.2 million and $626,000, respectively, for the change in the fair value of the redeemable convertible preferred stock liability in the consolidated statements of operations. There were no such charges incurred for the year ended December 31, 2017.

Note 12. Common Stock

The Company had reserved shares of common stock for issuance as follows:

	December 31,	
	2017	2016
Options issued and outstanding	2,438,151	2,393,829
Options available for future grants	531,039	164,328
ESPP shares available for future grants	268,554	150,000
Total	3,237,744	2,708,157

Note 13. Equity Plans

Equity Incentive Plan

In May 2007, the Company established the 2007 Stock Option and Incentive Plan ("2007 Plan") which provided for the granting of stock options to employees and consultants of the Company. Options granted under the 2007 Plan were either incentive stock options (ISOs) or nonqualified stock options (NSOs). ISOs were granted only to Company employees (including officers and directors who are also employees). NSOs were granted to Company employees and consultants. Options under the 2007 Plan have a term of ten years and generally vest over a four-year period with one-year cliff vesting.

In July 2016, the Company's board of directors and stockholders approved the 2016 Equity Incentive Plan ("2016 Plan") to replace the 2007 Plan, which became effective upon the IPO. Under the 2016 Plan, 1,200,000 shares of the Company's common stock were initially reserved for the issuance of stock options, restricted stock units and other awards to employees, directors and consultants. Pursuant to the "evergreen" provision contained in the 2016 Plan, the number of shares reserved for issuance under the 2016 Plan automatically increases on January 1 of each year, starting on January 1, 2017 and continuing through (and including) January 1, 2026, by 4% of the total number of shares of the Company's capital stock outstanding on December 31 of the preceding fiscal year, or a lesser number of shares determined by the Company's board of directors. Upon adoption of the 2016 Plan, no additional stock awards were issued under the 2007 Plan. Options granted under the 2007 Plan that were outstanding on the date the 2016 Plan became effective remain subject to the terms of the 2007 Plan. The number of options available for grant under the 2007 Plan was ceased and the number was added to the common stock reserved for issuance under the 2016 Plan. As of December 31, 2017, the Company has reserved 1,868,891 shares of common stock for issuance under the 2016 Plan.

The 2016 Plan is administered by the board of directors or a committee appointed by the board of directors, which determines the types of awards to be granted, including the number of shares subject to the awards, the exercise price and the vesting schedule. Options granted under the 2016 Plan expire no later than ten years from the date of grant. The exercise price of each option may not be less than 100% of the fair market value of the common stock at the date of grant. Options may be granted to stockholders possessing more than 10% of the total combined voting power of all classes of stocks of the Company at an exercise price at least 110% of the fair value of the common stock at the date of grant and the options are not exercisable after the expiration of 10 years from the date of grant. Employee stock options generally vest 25% upon one year of continued service to the Company, with the remainder in monthly increments over three additional years. Non-employee director initial stock options generally vest monthly over a period of approximately three years, and non-employee director annual refresher stock options generally vest over a period of approximately one year.

Stock Options

Activity under the Company's equity incentive plans 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 (1) (in millions)
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	
Additional options authorized	1,697,088	—			
Options granted	(1,679,979)	1,679,979	14.24		
Options exercised	—	(119,328)	1.28		
Balances at December 31, 2016	164,328	2,393,829	10.39	8.79	
Additional options authorized	668,891	—			
Options granted	(493,500)	493,500	13.20		
Options exercised	—	(257,858)	1.84		
Options forfeited	191,320	(191,320)	15.00		
Balances at December 31, 2017	531,039	2,438,151	$ 11.51	8.26	$ 23.3
Options exercisable – December 31, 2017		877,888	$ 9.70	7.61	$ 10.0
Options vested and expected to vest – December 31, 2017		2,438,151	$ 11.51	8.26	$ 23.3

(1) The aggregate intrinsic values were calculated as the difference between the exercise price of the options and the closing price of the Company's common stock on December 31, 2017. The calculation excludes options with an exercise price higher than the closing price of the Company's common stock on December 31, 2017.

The aggregate intrinsic value of options exercised was $3.5 million and $169,000 for the years ended December 31, 2017 and 2016, respectively. The aggregate intrinsic value of options exercised was immaterial for the year ended December 31, 2015.

During the years ended December 31, 2017, 2016 and 2015, the estimated weighted-average grant-date fair value of common stock underlying options granted was $7.74, $8.20 and $0.69 per share, respectively.

Employee Stock Options Valuation

The fair value of employee and non-employee 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,		
	2017	2016	2015
Expected term (in years)	5.50 – 6.08	4.16 – 5.95	5.89
Expected volatility	61.6% – 65.4%	62.5% – 64.8%	59.8%
Risk-free interest rate	1.88% – 2.24%	1.27% – 1.79%	1.57% – 1.58%
Dividend yield	—	—	—

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 does not have a long trading history for its common stock, the expected volatility is 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.

Prior to the completion of the Company's IPO, the fair value of the Company's shares of common stock underlying its stock options had historically been determined by the Company's board of directors. Because there had been no public market for the Company's common stock prior to August 2016, the Company's board of directors had 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. For stock options granted after the completion of the IPO, the Company's board of directors determined the fair value of each share of underlying common stock based on the closing price of the Company's common stock as reported on the date of grant.

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 to non-employees was calculated at each reporting date using the Black-Scholes option-pricing model with the following assumptions:

	Year Ended December 31,		
	2017	2016	2015
Expected term (in years)	6.97 – 7.40	6.59 – 9.97	6.80
Expected volatility	61.7% – 65.4%	62.5% – 62.8%	59.8%
Risk-free interest rate	2.17% – 2.33%	1.29% – 1.79%	1.95%
Dividend yield	—	—	—

During the years ended December 31, 2016 and 2015, the Company granted 59,647 and 4,816 shares, respectively, to non-employee consultants. No options were granted to non-employee consultants during the year ended December 31, 2017. The Company recorded stock-based compensation expense for non-employee awards during the years ended December 31, 2017, 2016 and 2015 of $263,000, $505,000 and $15,000, respectively.

Employee Stock Purchase Plan

In July 2016, the Company's board of directors and stockholders approved the 2016 Employee Stock Purchase Plan ("2016 ESPP"), which became effective upon the IPO. The 2016 ESPP is intended to qualify as an employee stock

purchase plan under Section 423 of the Internal Revenue Code of 1986, as amended, and is administered by the Company's board of directors and the Compensation Committee of the board of directors. Under the 2016 ESPP, 150,000 shares of the Company's common stock were initially reserved for employee purchases of the Company's common stock. Pursuant to the "evergreen" provision contained in the 2016 ESPP, the number of shares reserved for issuance automatically increases on January 1 of each year, starting on January 1, 2017 and continuing through (and including) January 1, 2026 by the lesser of (i) 1% of the total number of shares of common stock outstanding on December 31 of the preceding fiscal year (ii) 300,000 shares, or (iii) such other number of shares determined by the board of directors. The 2016 ESPP allows eligible employees to purchase shares of the Company's common stock at a discount through payroll deductions of up to 15% of their eligible compensation. At the end of each offering period, eligible employees are able to purchase shares at 85% of the lower of the fair market value of the Company's common stock at the beginning of the offering period or at the end of each applicable purchase period. As of December 31, 2017, a total of 317,222 shares were reserved for issuance under the 2016 ESPP, 48,668 shares have been issued, and 268,554 shares are available for issuance.

The fair value of the rights granted under the 2016 ESPP was calculated using the Black-Scholes option-pricing model with the following assumptions:

	Year Ended December 31,	
	2017	2016
Expected term (in years)	0.50	0.60
Expected volatility	52.43% – 52.44%	52.48%
Risk-free interest rate	0.89% – 1.16%	0.45%
Dividend yield	—	—

Stock-Based Compensation

Total stock-based compensation expense was as follows (in thousands):

	Year Ended December 31,		
	2017	2016	2015
Research and development	$ 2,008	$ 1,080	$ 39
General and administrative	2,233	1,050	60
Total stock-based compensation expense	$ 4,241	$ 2,130	$ 99

As of December 31, 2017, total unrecognized stock-based compensation expense was $10.7 million, which the Company expects to recognize over a period of approximately 2.46 years.

Note 14. 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.

Note 15. Income Taxes

No provision for income taxes was recorded for the years ended December 31, 2017, 2016 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.

The following table presents domestic and foreign components of net loss for the periods presented (in thousands):

	Year Ended December 31,		
	2017	2016	2015
Domestic	$ (34,556)	$ (34,977)	$ (10,483)
Foreign	(2,401)	(2,200)	(4,375)
Total net loss	$ (36,957)	$ (37,177)	$ (14,858)

The effective tax rate of the provision for income taxes differs from the federal statutory rate as follows:

	Year Ended December 31,		
	2017	2016	2015
Federal statutory income tax rate	34.0 %	34.0 %	34.0 %
State taxes, net of federal benefit	0.5	6.5	(2.7)
Warrant revaluation	—	(4.3)	(0.2)
Research credit	2.6	1.8	1.1
Foreign tax rate difference	(1.2)	(1.6)	(11.8)
Change in tax law	(31.2)	—	—
Change in valuation allowance	(5.2)	(36.0)	(19.9)
Other	0.5	(0.4)	(0.5)
Provision for income taxes	— %	— %	— %

On December 22, 2017, the Tax Cuts and Jobs Act of 2017 ("Tax Act") was signed into law making significant changes to the Internal Revenue Code. Changes include, but are not limited to, a corporate tax rate decrease from 35% to 21% effective for tax years beginning after December 31, 2017, the transition of U.S. international taxation from a worldwide tax system to a territorial system, and a one-time transition tax on the mandatory deemed repatriation of cumulative foreign earnings as of December 31, 2017.

The corporate tax rate reduction to 21% under the Tax Act is effective January 1, 2018. Consequently, the Company has recorded a decrease in net deferred tax assets of $11.5 million, with a corresponding adjustment to the valuation allowance of $11.5 million, for the year ended December 31, 2017. The state deferred tax effect on federal deferred tax assets has been calculated using 79% rather than the previous 66% federal benefit. The increase in deferred tax assets has been offset against an increase to the valuation allowance.

The Deemed Repatriation Transition Tax ("Transition Tax") is a tax on previously untaxed accumulated and current earnings and profits ("E&P") of certain foreign subsidiaries. To determine the amount of the Transition Tax, the Company must determine, in addition to other factors, the amount of post-1986 E&P of the relevant subsidiaries, as well as the amount of non-U.S. income taxes paid on such earnings. Since Protagonist Pty Limited, the Company's only foreign subsidiary, has a cumulative deficit in E&P, there is no Transition Tax to be included in the December 31, 2017 tax provision.

On December 22, 2017, the SEC staff issued Staff Accounting Bulletin No. 118 ("SAB 118"), which provides guidance for the tax effect of the Tax Act. SAB 118 provides a measurement period that should not extend beyond one year from the Tax Act's enactment date for companies to complete the accounting under Accounting Standards Codification Topic 740, *Income Taxes* ("ASC 740"). In accordance with SAB 118, the Company must reflect the income tax effects of those aspects of the Tax Act for which the accounting under ASC 740 is complete. To the extent that the Company's accounting for certain income tax effects of the Tax Act is incomplete, but it is able to determine a reasonable estimate, the Company must record a provisional estimate in its consolidated financial statements. If the Company cannot determine a provisional estimate to be included in its consolidated financial statements, it should continue to apply ASC 740 on the basis of the provisions of the tax laws that were in effect immediately before the enactment of the Tax Act. The amounts of the tax effects related to the Tax Act described in the paragraphs above represent the Company's reasonable estimates and are provisional amounts within the meaning of SAB 118. The provisional transition tax at zero has been determined based on the cumulative deficit foreign E&P as of the relevant measurement date. Any change to such estimate during the measurement period should have no material impact on the

Company's financial statements. Also, it is expected that the U.S. Treasury will issue regulations and other guidance on the application of certain provisions of the Tax Act. In subsequent periods, but within the measurement period, the Company will analyze that guidance and other necessary information to refine its estimates and complete its accounting for the tax effects of the Tax Act as necessary.

In January 2018, the FASB released guidance on the accounting for tax on the global intangible low-taxed income ("GILTI") provisions of the Tax Act. The GILTI provisions impose a tax on foreign income in excess of a deemed return on tangible assets of foreign corporations. The guidance indicates that either accounting for deferred taxes related to GILTI inclusions or treating any taxes on GILTI inclusions as a period cost are both acceptable methods subject to an accounting policy election. Effective for the quarter ending March 31, 2018, the Company will elect to treat any potential GILTI inclusions as a period cost as the Company is not projecting any material impact from GILTI inclusions and any deferred taxes related to any inclusion would be immaterial.

The components of the deferred tax assets are as follows (in thousands):

	December 31,	
	2017	2016
Deferred tax assets:		
Net operating loss carryforwards	$ 21,682	$ 21,501
Depreciation and amortization	339	419
Accruals/other	1,322	908
Research and development credits and foreign credits	2,544	1,143
Total deferred tax assets	25,887	23,971
Valuation allowance	(25,887)	(23,971)
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, 2017 and 2016 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 $1.9 million, $13.4 million and $3.0 million during the years ended December 31, 2017, 2016 and 2015, respectively. The current year change in the valuation allowance is mainly related to the increase in net operating loss carryforwards generated during the year and offset by a decrease in the deferred tax assets related to the reduction of the U.S. corporate income tax rate as provided in the Tax Act. The increase in valuation allowance in the prior years in mainly related to the increase in net operating loss carryforwards incurred during the respective taxable years.

At December 31, 2017, the Company had net operating loss carryforwards for federal income tax purposes of approximately $79.2 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 $68.0 million which are available to offset future taxable income, if any, through 2033.

At December 31, 2017 the Company also had accumulated Australian tax losses of $10.4 million available for carry forward against future earnings which, under relevant tax laws, do not expire but may be limited under certain circumstances.

As of December 31, 2017, the Company also had $2.4 million of federal and $1.3 million of state research and development tax credit carryforwards available to reduce future income taxes. The federal research and development tax credits will begin to expire in 2035, if not utilized. The state research and development tax credits have no expiration date.

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 benefit of tax losses and tax credits that existed at the time of the ownership change may be significantly reduced. Based on a review of the

Company's equity transactions since inception, the Company believes a portion of its net operating loss carryforwards and credit carryforwards may be limited due to an equity financing which occurred in 2015.

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,		
	2017	2016	2015
Balance at beginning of year	$ 2,131	$ 805	$ —
Additions based on tax positions related to prior years	—	707	690
Additions based on tax positions related to current year	3,283	619	115
Balance at end of year	$ 5,414	$ 2,131	$ 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 2013 through 2017 remain open for examination due to the carryover of unused net operating losses and tax credits.

Note 16. Net Loss per Share Attributable to Common Stockholders

As the Company had net losses for the years ended December 31, 2017, 2016 and 2015, all potential common shares were determined to be anti-dilutive. The following table sets forth the computation of basic and diluted net loss per share attributable to common stockholders (in thousands, except share and per share data):

	Year Ended December 31,		
	2017	2016	2015
Numerator:			
Net loss	$ (36,957)	$ (37,177)	$ (14,858)
Accretion of redeemable convertible preferred stock	—	(558)	(75)
Net loss attributable to common stockholders	$ (36,957)	$ (37,735)	$ (14,933)
Denominator:			
Weighted-average shares used to compute net loss per common share, basic and diluted	17,694,505	6,501,796	251,717
Net loss per share attributable to common stockholders, basic and diluted	$ (2.09)	$ (5.80)	$ (59.32)

The following outstanding shares of potentially dilutive securities have been excluded from diluted net loss per share calculations for the years ended December 31, 2017, 2016 and 2015 because their inclusion would be anti-dilutive:

	Year Ended December 31,		
	2017	2016	2015
Options to purchase common stock	2,438,151	2,393,829	833,178
ESPP shares	24,938	—	—
Redeemable convertible preferred stock on an as-converted basis	—	—	5,323,103
Warrants to purchase redeemable convertible preferred stock on an as-converted basis	—	—	275,861
Total	2,463,089	2,393,829	6,432,142

Note 17. Supplementary Financial Data (unaudited)

The following table presents the selected quarterly financial data for the years ended December 31, 2017 and 2016:

	Consolidated Statements of Operations			
	Quarter Ended			
	March 31	June 30	September 30	December 31
	(In thousands, except per share amounts)			
2017				
License and collaboration revenue - related party	$ —	$ —	$ 8,781	$ 11,282
Loss from operations	$ (14,273)	$ (15,131)	$ (4,980)	$ (3,513)
Net loss	$ (14,101)	$ (14,979)	$ (4,825)	$ (3,052)
Net loss per share of common stock attributable to common stockholders, basic and diluted (1)	$ (0.84)	$ (0.89)	$ (0.29)	$ (0.15)
2016				
Loss from operations	$ (7,040)	$ (7,091)	$ (7,138)	$ (11,397)
Net loss	$ (11,747)	$ (7,098)	$ (7,084)	$ (11,248)
Net loss per share of common stock attributable to common stockholders, basic and diluted (1)	$ (40.96)	$ (19.07)	$ (0.87)	$ (0.67)

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

None.

Item 9A. Controls and Procedures

Evaluation of disclosure controls and procedures

Management, under the supervision and with the participation of our Chief Executive Officer and Chief Financial Officer, has evaluated the effectiveness of our disclosure controls and procedures (as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act) as of December 31, 2017. Based on the evaluation of our disclosure controls and procedures, our Chief Executive Officer and Chief Financial Officer have concluded that our disclosure controls and procedures as of December 31, 2017 were effective at the reasonable assurance level.

Management's annual report on internal control over financial reporting.

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act. Our management, including our Chief Executive Officer and Chief Financial Officer, conducted an evaluation of the effectiveness of our internal control over financial reporting based on the criteria set forth in *Internal Control-Integrated Framework* (2013) issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on its evaluation under the criteria set forth in *Internal Control-Integrated Framework*, our management concluded that our internal control over financial reporting was effective as of December 31, 2017.

This annual report does not include an attestation report of the Company's registered public accounting firm regarding internal control over financial reporting. Management's report was not subject to attestation by the Company's registered public accounting firm pursuant to rules of the Securities and Exchange Commission that permit the Company to provide only management's report in this Annual Report on Form 10-K.

Remediation of Material Weaknesses

In connection with the audit of our consolidated financial statements for the years ended December 31, 2015 and 2014, 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 resulted in the identification of a second material weakness in our internal control over financial reporting for the years ended December 31, 2015 and 2014, which continued to exist as of December 31, 2016. Specifically, we did not, and had not historically, appropriately design and implement controls over the review and approval of manual journal entries and the related supporting journal entry calculations.

Our plan to remediate the material weaknesses, included implementing a new accounting software system, configuring the software to support the approval of manual journal entries and adding additional accounting personnel was completed as of December 31, 2017. We completed the implementation of a new accounting system during the first quarter of 2017 to improve our information systems related controls. We have added additional finance and accounting personnel as needed to enhance segregation of duties and we have utilized consultants with technical accounting expertise as needed. Accordingly, management determined that the material weaknesses have been remediated as of December 31, 2017.

Changes in internal control over financial reporting

There have been no changes in our internal control over financial reporting that occurred during our most recent fiscal quarter that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

None.

PART III

Item 10. Directors, Executive Officers, and Corporate Governance

Except as set forth below, the information required by this item is incorporated by reference from our definitive Proxy Statement to be filed with the SEC in connection with our 2018 Annual Meeting of Stockholders within 120 days after the end of the fiscal year ended December 31, 2017.

We have adopted a Code of Business Conduct and Ethics that applies to all of our directors, officers and employees, including our principal executive officer and principal financial officer. The Code of Business Conduct and Ethics is posted on our website at www.protagonist-inc.com.

We intend to satisfy the disclosure requirement under Item 5.05 of Form 8-K regarding an amendment to, or waiver from, a provision of this Code of Business Conduct and Ethics by posting such information on our website, at the address and location specified above and, to the extent required by the listing standards of The Nasdaq Global Market, by filing a Current Report on Form 8-K with the SEC, disclosing such information.

Item 11. Executive Compensation

The information required by this item is incorporated by reference from our definitive Proxy Statement to be filed with the SEC in connection with our 2018 Annual Meeting of Stockholders within 120 days after the end of the fiscal year ended December 31, 2017.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters

The information required by this item is incorporated by reference from our definitive Proxy Statement to be filed with the SEC in connection with our 2018 Annual Meeting of Stockholders within 120 days after the end of the fiscal year ended December 31, 2017.

Item 13. Certain Relationships and Related Transactions, and Director Independence

The information required by this item is incorporated by reference from our definitive Proxy Statement to be filed with the SEC in connection with our 2018 Annual Meeting of Stockholders within 120 days after the end of the fiscal year ended December 31, 2017.

Item 14. Principal Accounting Fees and Services

The information required by this item is incorporated by reference from our definitive Proxy Statement to be filed with the SEC in connection with our 2018 Annual Meeting of Stockholders within 120 days after the end of the fiscal year ended December 31, 2017.

PART IV

Item 15. Exhibits, Financial Statement Schedules

(a) The following documents are filed as part of this report:

(1) FINANCIAL STATEMENTS

The financial statements filed as part of this Annual Report on Form 10-K are included in Part II, Item 8 of this Annual Report on Form 10-K.

(2) FINANCIAL STATEMENT SCHEDULES

Financial statement schedules have been omitted in this Annual Report on Form 10-K because they are not applicable, not required under the instructions, or the information requested is set forth in the financial statements or related notes thereto.

(3) EXHIBITS

The exhibits listed in the accompanying Exhibit Index are filed as part of, or incorporated by reference into, this Annual Report on Form 10-K.

EXHIBIT INDEX

Exhibit Number	Exhibit Description	Incorporation By Reference				Filed Herewith
		Form	SEC File No.	Exhibit	Filing Date	
3.1	Amended and Restated Certificate of Incorporation	8-K	00137852	3.1	8/16/2016	
3.2	Amended and Restated Bylaws	S-1/A	333212476	3.2	8/1/2016	
4.1	Specimen stock certificate evidencing the shares of common stock	S-1/A	333212476	4.1	8/1/2016	
4.2	Third Amended and Restated Investor Rights Agreement, by and among Protagonist Therapeutics, Inc. and the stockholders named therein, dated July 31, 2016.	S-1/A	333212476	4.2	8/1/2016	
4.3	Form of Indenture	S-3	333-220314	4.5	9/1/2017	
10.1+	Protagonist Therapeutics, Inc. 2007 Stock Option and Incentive Plan, as amended and restated, and form of option agreement, exercise notice, joinder, and adoption agreement thereunder.	S-1	333212476	10.1	7/11/2016	
10.2+	Protagonist Therapeutics, Inc. 2016 Equity Incentive Plan and forms of stock option grant notice, option agreement, notice of exercise, restricted stock unit grant notice and restricted stock unit agreement thereunder.	S-1/A	333212476	10.2	8/1/2016	
10.3+	Protagonist Therapeutics, Inc. 2016 Employee Stock Purchase Plan.	S-1/A	333212476	10.3	8/1/2016	
10.4+	Form of Indemnity Agreement for Directors and Officers.	S-1/A	333212476	10.4	8/1/2016	
10.5	Lease, dated September 30, 2013, by and between the Registrant and Berrueta Family Partnership.	S-1	333212476	10.5	7/11/2016	

Exhibit Number	Exhibit Description	Incorporation By Reference				Filed Herewith
		Form	SEC File No.	Exhibit	Filing Date	
10.6	First Amendment to Lease, dated March 24, 2014, by and between the Registrant and Berrueta Family Partnership.	S-1	333212476	10.6	7/11/2016	
10.7	Second Amendment to Lease, dated May 4 2015, by and between the Registrant and Berrueta Family L.P.	S-1	333212476	10.7	7/11/2016	
10.8	Third Amendment to Lease, dated August 11, 2015, by and between the Registrant and Berrueta Family L.P.	S-1	333212476	10.8	7/11/2016	
10.9	Lease, dated March 6, 2017, by and between the Registrant and BMR-Pacific Research Center LP.	10-K	001-37852	10.9	3/7/2017	
10.10+	Severance Agreement, dated August 1, 2016, by and between the Registrant and Dinesh Patel.	S-1/A	333212476	10.9	8/1/2016	
10.11+	Severance Agreement, dated August 1, 2016, by and between the Registrant and David Y. Liu, Ph.D.	S-1/A	333212476	10.10	8/1/2016	
10.12+	Severance Agreement, dated August 1, 2016, by and between the Registrant and Tom O'Neil.	S-1/A	333212476	10.12	8/1/2016	
10.13+	Severance Agreement, dated August 1, 2016, by and between the Registrant and Richard Shames, M.D.	S-1/A	333212476	10.13	8/1/2016	
10.14†	Research and Collaboration Agreement, dated June 16, 2012, by and among the Registrant, Protagonist Pty. Ltd. and Zealand Pharma A/S.	S-1	333212476	10.17	7/11/2016	
10.15†	Contract Extension Letter of Agreement, dated June 1, 2013, by and among the Registrant, Protagonist Pty. Ltd. and Zealand Pharma A/S.	S-1	333212476	10.18	7/11/2016	
10.16†	Agreement on Addition of Additional Collaboration Program, dated September 16, 2013, by and among the Registrant, Protagonist Pty. Ltd. and Zealand Pharma A/S.	S-1	333212476	10.19	7/11/2016	
10.17†	Protagonist Assumption of Responsibility, dated January 28, 2014, by and between the Registrant and Zealand Pharma A/S.	S-1	333212476	10.20	7/11/2016	
10.18†	Agreement to Assign Patent Applications, dated February 7, 2014, by and between the Registrant, Protagonist Pty. Ltd. and Zealand Pharma A/S.	S-1	333212476	10.21	7/11/2016	
10.19†	Abandonment Agreement, dated February 28, 2014, by and among the Registrant, Protagonist Pty. Ltd. and Zealand Pharma A/S.	S-1	333212476	10.22	7/11/2016	
10.20†	Exclusive License and Collaboration Agreement, dated May 26, 2017, by and between the Registrant and Janssen Biotech, Inc.	8-K/A	001-37852	10.1	7/31/2017	
10.21	Sales Agreement, dated September 1, 2017, by and between the Registrant and Cantor Fitzgerald & Co.	S-3	333-220314	1.2	9/1/2017	
21.1	List of Subsidiaries					X
23.1	Consent of Independent Registered Public Accounting Firm					X
24.1	Power of Attorney (included in signature page of this Form 10-K)					X

Exhibit Number	Exhibit Description	Incorporation By Reference				Filed Herewith
		Form	SEC File No.	Exhibit	Filing Date	
31.1	Certification of Chief Executive Officer required by Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002					X
31.2	Certification of Chief Financial Officer required by Rule 13a-14(a) or Rule 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002					X
32.1*	Certification of Chief Executive Officer and Chief Financial Officer, as required by Rule 13a-14(b) or Rule 15d-14(b) and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350), as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002					X
101.INS	XBRL Instance Document					X
101.SCH	XBRL Taxonomy Extension Schema Document					X
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document					X
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document					X
101.LAB	XBRL Taxonomy Extension Labels Linkbase Document					X
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document					X

+ Indicates management contract or compensatory plan, contract or agreement.
† Confidential treatment has been granted for a portion of this exhibit.
* This certification attached as Exhibit 32.1 that accompanies this Annual Report on Form 10-K is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of Protagonist Therapeutics, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date of the Form 10-K, irrespective of any general incorporation language contained in such filing.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

PROTAGONIST THERAPEUTICS, INC.

Date: March 7, 2018

By: /s/ Dinesh V. Patel, Ph.D.
Dinesh V. Patel, Ph.D.
President, Chief Executive Officer and Director
(Principal Executive Officer)

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Dinesh V. Patel and Thomas P. O'Neil, and each of them, his true and lawful attorneys-in-fact, with full power of substitution, for him in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, and to file the same, with exhibits thereto and other documents in connection therewith with the Securities and Exchange Commission, hereby ratifying and confirming all that said attorneys-in-fact or any of them or their substitute or substitutes may lawfully do or cause to be done by virtue thereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant in the capacities and on the dates indicated:

Signature	Title	Date
/s/ Dinesh V. Patel, Ph.D. Dinesh V. Patel, Ph.D.	President, Chief Executive Officer and Director *(Principal Executive Officer)*	March 7, 2018
/s/ Thomas P. O'Neil Thomas P. O'Neil	Chief Financial Officer *(Principal Financial and Accounting Officer)*	March 7, 2018
/s/ Harold E. Selick, Ph.D. Harold E. Selick, Ph.D.	Chairman of the Board of Directors	March 7, 2018
/s/ Chaitan Khosla, Ph.D. Chaitan Khosla, Ph.D.	Director	March 7, 2018
/s/ Sarah M. Noonberg, M.D., Ph.D. Sarah M. Noonberg, M.D., Ph.D.	Director	March 7, 2018
/s/ Armen Shanafelt, Ph.D. Armen Shanafelt, Ph.D.	Director	March 7, 2018
/s/ William D. Waddill William D. Waddill	Director	March 7, 2018
/s/ Lewis T. Williams, M.D., Ph.D. Lewis T. Williams, M.D., Ph.D.	Director	March 7, 2018

Exhibit 21.1

SUBSIDIARIES OF PROTAGONIST THERAPEUTICS, INC.

Subsidiary	Jurisdiction of Formation/Organization
Protagonist Pty Limited	Australia

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statements on Forms S-8 (No. 333-213120 and No. 333-216532) and Form S-3 (No. 333-220314) of Protagonist Therapeutics, Inc. of our report dated March 7, 2018 relating to the consolidated financial statements, which appears in this Form 10-K.

/s/ PricewaterhouseCoopers LLP

San Jose, CA
March 7, 2018

Exhibit 31.1

CERTIFICATION OF CHIEF EXECUTIVE OFFICER
Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002

I, Dinesh V. Patel, certify that:

1. I have reviewed this Annual Report on Form 10-K of Protagonist Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and we have:

   a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an Annual Report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 7, 2018

/s/ Dinesh V. Patel, Ph.D.
Dinesh V. Patel, Ph.D.
President, Chief Executive Officer

Exhibit 31.2

CERTIFICATION OF CHIEF FINANCIAL OFFICER
Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002

I, Thomas P. O'Neil, certify that:

1. I have reviewed this Annual Report on Form 10-K of Protagonist Therapeutics, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and we have:

   a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an Annual Report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

/s/ Thomas P. O'Neil
Thomas P. O'Neil
Chief Financial Officer

Date: March 7, 2018

Exhibit 32.1

CERTIFICATION OF CHIEF EXECUTIVE OFFICER AND CHIEF FINANCIAL OFFICER

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended, (the "Exchange Act") and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. §1350), Dinesh V. Patel, Chief Executive Officer of Protagonist Therapeutics, Inc. (the "Company"), and Thomas P. O'Neil, Chief Financial Officer of the Company, each hereby certify that, to the best of his knowledge:

1. The Company's Annual Report on Form 10-K for the period ended December 31, 2017 (the "Annual Report"), to which this Certification is attached as Exhibit 32.1, fully complies with the requirements of Section 13(a) or Section 15(d) of the Exchange Act; and

2. The information contained in the Annual Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 7, 2018

/s/ Dinesh V. Patel, Ph.D.
Dinesh V. Patel, Ph.D.
President, Chief Executive Officer

Date: March 7, 2018

/s/ Thomas P. O'Neil
Thomas P. O'Neil
Chief Financial Officer

This certification accompanies the Form 10-K to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of Protagonist Therapeutics, Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Form 10-K), irrespective of any general incorporation language contained in such filing.