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, 2019

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.)**
7707 Gateway Boulevard, Suite 140 Newark, California 94560	
(Address, including zip code, of registrant's principal executive offices)	**(510) 474-0170 (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	**Trading Symbol**	**Name of each exchange on which registered**
Common Stock, $0.00001 par value	**PTGX**	**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 every Interactive Data File required to be submitted 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 such files). 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 an 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	☐	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 $212.4 million as of June 30, 2019, based upon the closing sale price on The Nasdaq Global Market reported on June 30, 2019. Excludes an aggregate of 7,424,570 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, 2019, the registrant assumed that a stockholder was an affiliate of the registrant at June 30, 2019 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, 2019. 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 27,294,299 shares of registrant's Common Stock, par value $0.00001 per share, outstanding as of February 28, 2020.

DOCUMENTS INCORPORATED BY REFERENCE:

Portions of the registrant's definitive Proxy Statement for the registrant's 2020 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, 2019.

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PART I

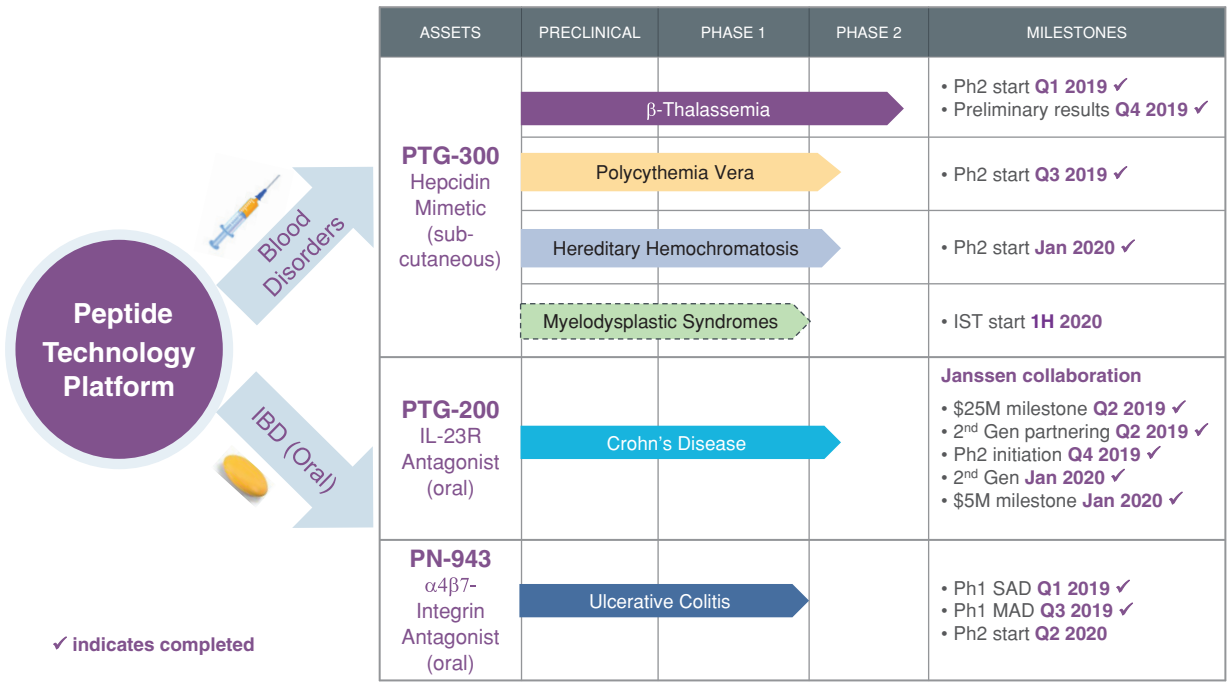
Statements made in this Annual Report on Form 10-K contain certain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. Forward-looking statements are identified by words such as "believe," "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.

Overview

We are a clinical-stage biopharmaceutical company that utilizes a proprietary technology platform to discover and develop novel peptide-based drugs to address significant unmet medical needs and transform existing treatment paradigms for patients. We have three assets in various stages of clinical development derived from this platform, and we expect to report results from six different Phase 2 studies by the end of 2021.

Figure 1: Our Product Pipeline



Our most advanced clinical asset, PTG-300, is an injectable hepcidin mimetic in development for the potential treatment of iron overload and other blood disorders. PTG-300 mimics the effect of the natural hormone hepcidin, but with greater potency, solubility and stability. Hepcidin is a key hormone in regulating iron equilibrium and is critical to the proper development of red blood cells. We are currently developing PTG-300 for the treatment of ineffective erythropoiesis, chronic anemia and iron overload, with an initial focus on beta-thalassemia non-transfusion dependent ("NTD") and transfusion dependent ("TD") patients where the primary endpoints are hemoglobin increases and transfusion burden reductions, respectively. PTG-300 has received an orphan drug designation from the U.S. Food and Drug Administration ("FDA") and European Union ("EU") regulatory authorities for the treatment of beta-thalassemia. The FDA has granted Fast Track designation to PTG-300 for the treatment of beta-thalassemia. In the first quarter of 2019, we began dosing patients in a global Phase 2 study of PTG-300 in beta-thalassemia. Preliminary results from this Phase 2 study reported in the fourth quarter of 2019 suggest that the dose related pharmacodynamic responses in lowering serum iron and transferrin saturation ("TSAT") warrant continued evaluation at higher and/or more frequent doses which will be required to evaluate the rate and durability of clinical response in order to reach definitive conclusions. We expect to report clinical efficacy results from this Phase 2 study in 2020. We initiated a Phase 2 study in polycythemia vera ("PV") in the third quarter of 2019 and a Phase 2 study in hereditary hemochromatosis ("HH") in January 2020. We are working toward the initiation of an investigator-sponsored study ("IST") of PTG-300 in patients with myelodysplastic syndromes ("MDS") in the first half of 2020. Assuming PTG-300 shows clinical efficacy in one or more of the above indications, we intend to select our first indication in 2020 for a potential pivotal study to begin in 2021.

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

PTG-200 (also referenced as JNJ-67864238) is an orally delivered gut-restricted Interleukin-23 receptor ("IL-23R") antagonist for the treatment of IBD. In May 2017, we entered into a worldwide license and collaboration agreement with Janssen Biotech, Inc. ("Janssen"), a Johnson & Johnson company, to co-develop and co-detail PTG-200 and any second-generation compounds for all indications, including IBD. The agreement with Janssen was amended in May 2019 to expand the collaboration by supporting efforts towards second-generation IL-23R antagonists, triggering a $25.0 million milestone payment to us. In January 2020, as part of the expanded research collaboration, we announced the identification and nomination of an orally delivered, gut-restricted IL-23R antagonist peptide as a second-generation development candidate, triggering a $5.0 million milestone payment to us. 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. In 2018, we completed a Phase 1 clinical study to evaluate the safety, pharmacokinetics and pharmacodynamics of PTG-200 in healthy volunteers. Janssen submitted a U.S. Investigational New Drug application ("IND") for PTG-200 in CD during the second quarter of 2019, which took effect in July 2019. In collaboration with Janssen, we initiated a Phase 2 clinical study for PTG-200 in CD in the fourth quarter of 2019, with results expected in the first half of 2021.

PN-943 is an orally delivered, gut-restricted, alpha-4-beta-7 ("α4β7") specific integrin antagonist. We developed PN-943 as a potentially more potent orally delivered, gut-restricted α4β7 backup compound to PTG-100, our first-generation orally delivered gut-restricted α4β7 inhibitor that was being developed for treatment of UC. In 2019, we completed a Phase 1 single ascending dose ("SAD") and multiple ascending dose ("MAD") clinical study of PN-943 in healthy volunteers to evaluate safety, pharmacokinetics and pharmacodynamics. We reported results of the SAD part of the study during the second quarter of 2019 and the MAD part of the study during the third quarter of 2019. The pharmacodynamic results indicated that the administration of PN-943 was well tolerated, and results of target engagement were supportive of the higher potency of PN-943 as compared to PTG-100. We submitted a U.S. IND for PN-943 in December 2019, which took effect in January 2020. We anticipate initiating a Phase 2 proof of concept ("POC") study in UC in the second quarter of 2020, with topline data expected in the second half of 2021.

Our clinical assets are all derived from our proprietary discovery platform. Our platform enables us to engineer novel, structurally constrained peptides that retain key advantages of both orally delivered small molecules and injectable antibody drugs, while overcoming many of their limitations as therapeutic agents. Importantly, constrained peptides can be designed to alleviate the fundamental instability inherent in traditional peptides to allow different delivery forms, such as oral, subcutaneous, intravenous, and rectal. We continue to use our peptide technology platform to discover product candidates against targets in disease areas with significant unmet medical needs.

PTG-300: AN INJECTABLE HEPCIDIN MIMETIC

PTG-300, an injectable hepcidin mimetic, was discovered through our peptide technology platform. Hepcidin is a natural hormone that regulates iron metabolism. We are developing PTG-300 for the treatment of certain disorders characterized by ineffective erythropoiesis, excessive red blood cells or iron overload. In diseases of ineffective erythropoiesis, excessive quantities of iron in the bone marrow contribute to oxidative stress and premature cell death causing anemia. In healthy individuals, hepcidin regulates iron levels by inhibiting iron absorption from the GI tract and by limiting macrophage release of iron. Individuals with beta-thalassemia and MDS can have insufficient hepcidin to maintain appropriate iron levels that result in chronic anemia. Because of stability issues, complexity of synthesis and solubility limitations, direct replacement with native hepcidin is not a practical therapeutic approach. We developed PTG-300 as a stable, soluble, more readily manufactured injectable hepcidin mimetic that could potentially prevent iron toxicity and anemia with chronic subcutaneous injections.

Mechanism of Action and Rationale

The molecular target of the hormone 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 redistributes iron by reducing the export of iron from inside the enterocytes and macrophages to the systemic circulation. Excessive quantities of iron relative to the lower levels of beta-globin chains in the bone marrow induce ineffective erythropoiesis resulting in anemia. As a hepcidin mimetic, PTG-300 may redistribute iron to the macrophages, reduce iron-induced oxidative stress in the bone marrow, and allow 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 such as the liver and heart (i.e. secondary iron overload).

Iron Disorders Overview

Beta-thalassemia

Beta-thalassemia is a rare genetic blood disorder that is characterized by impaired red blood cell production. As a result of the underlying genetic defect in β-globin production, beta-thalassemia patients may be severely anemic, resulting in the need for lifelong supportive care with regular red blood cell transfusions. Repeated transfusions can cause secondary iron overload in the heart and liver which results in shortened lifespan in patients. In the bone marrow, elevated levels of iron relative to the decreased levels of beta-globin can prevent red blood cells from fully developing, resulting in anemia. In addition, the resulting immature red blood cells can aggregate in the spleen causing organ enlargement that may require surgical removal. In conditions of ineffective erythropoiesis, such as beta-thalassemia and MDS, hepcidin levels are suppressed leading to increases in iron absorption from the GI tract and iron export from macrophages which may be toxic to developing erythrocytes. It has been proposed that agents with hepcidin activity may help correct the iron distribution abnormalities in beta-thalassemia with beneficial effects on erythropoiesis.

Existing treatment options for iron-loading anemia and secondary iron overload are limited. Patients with transfusion-dependent ("TD") beta-thalassemia require lifelong regular red blood cell transfusions and general supportive care. 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 may require treatment with chelating agents, which can have adverse effects. Transfusion and iron chelation therapy have significantly improved the survival of TD beta-thalassemia patients over the last few decades. However, these agents work very slowly and have significant kidney, gastrointestinal, and liver toxicity issues. The greatest unmet need for beta-thalassemia is for more effective treatment for chronic anemia to decrease the burden of frequent blood transfusions and thus eliminate the complications associated with the disease and its management as well as costs associated with red blood cell transfusions and chelation therapy. We believe that PTG-300 may be able to restore iron homeostasis in the bone marrow as well as reduce excess circulating iron, improving anemia and thereby reducing or eliminating the need for red blood cell transfusions and related chelation treatments.

Beta-thalassemia is most prevalent in people of Mediterranean descent, such as Italians, Greeks or 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, with at least 60,000 patients born each year with the disease, according to the Centers for Disease Control and Prevention. In 2018, Decision Resource Group ("DRG") reported that while beta-thalassemia has a worldwide carrier rate of 1.5%, the disease is rare in the United States, Italy, Germany, United Kingdom, Spain, and France with a total diagnosed prevalence of 16,000 patients, approximately 85% of which are transfusion dependent, representing an estimated market opportunity of approximately $1.4 billion to $2.5 billion. The prevalence in the United States is low, with an estimated 3,000 patients and approximately 300 patients born each year with the disease. 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.

Polycythemia vera ("PV")

PV is a rare chronic disease caused by a hematopoietic stem cell mutation. PV is characterized by excessive erythropoiesis (production of blood cells). These excess blood cells can increase risk of serious problems such as blood clots, potentially leading to heart attack and stroke as well as more common symptoms including fatigue, headache, blurred vision, shortness of breath and an enlarged spleen. Over time PV may transform into myelofibrosis or leukemia. An important aspect of the mechanism of action of the hepcidin mimetic PTG-300 is to reduce serum iron, which is required to support the excessive erythropoiesis which occurs in PV, thereby potentially enabling PTG-300 to manage this excessive erythropoiesis and ultimately reduce the phlebotomy burden and thrombotic risk in these patients. In the United States, Italy, Germany, United Kingdom, Spain and France, there are currently more than 150,000 diagnosed PV patients representing an estimated market opportunity of approximately $1.0 billion to $2.0 billion.

Hereditary hemochromatosis ("HH")

HH is a blood disorder caused by genetic mutations that increase iron uptake from the diet and alter its distribution in the body, leading to iron buildup in the body's tissues and organs, particularly in the skin, heart, liver, pancreas and joint tissues. Excess iron in these organs and tissues can be toxic and over time lead to cirrhosis, liver cancer, heart problems, joint pain and diabetes. Current treatments for HH, including periodic phlebotomy, can be a significant burden to patients. PTG-300 could potentially reduce the need for phlebotomy and offer a safer and better long-term solution to management of the disease. The genetic defects that cause most HH are present in approximately five to seven million patients in the United States and EU.

Myelodysplastic syndromes ("MDS")

MDS are a group of disorders in which blood cells do not mature properly in the bone marrow. Symptoms can include fatigue, shortness of breath, excessive bleeding or frequent infections. There are approximately 19,000 transfusion dependent MDS patients in the United States, Italy, Germany, United Kingdom, Spain, and France. There are multiple MDS subpopulations, some of which are characterized by anemia, low hepcidin, and high serum iron and transferrin saturation. Significant unmet needs for these patients include reduction in or elimination of transfusions, prevention of disease progression to acute myelogenous leukemia and overall survival.

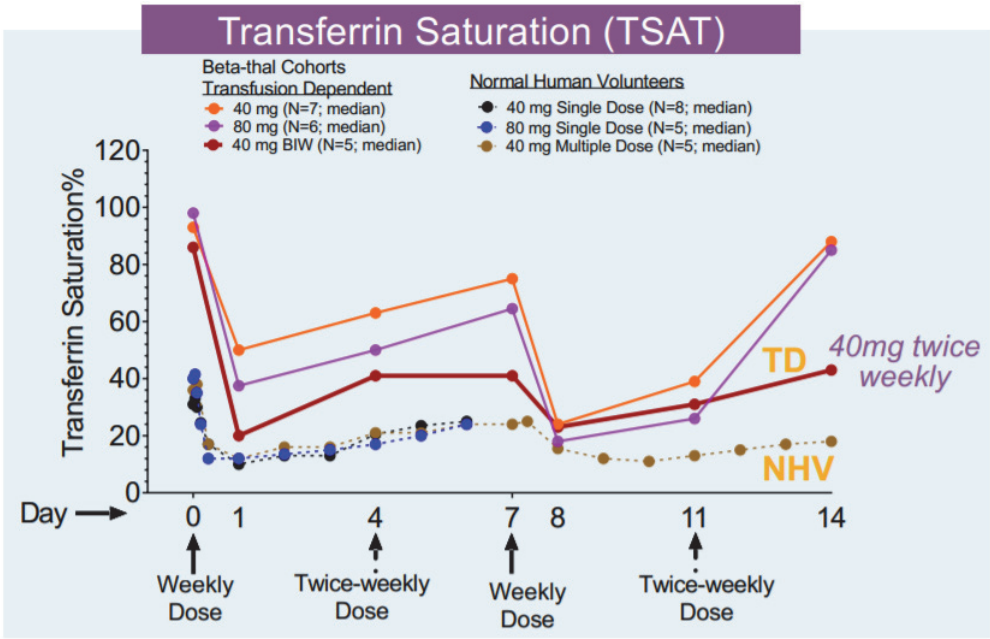
PTG-300's Clinical Development Program

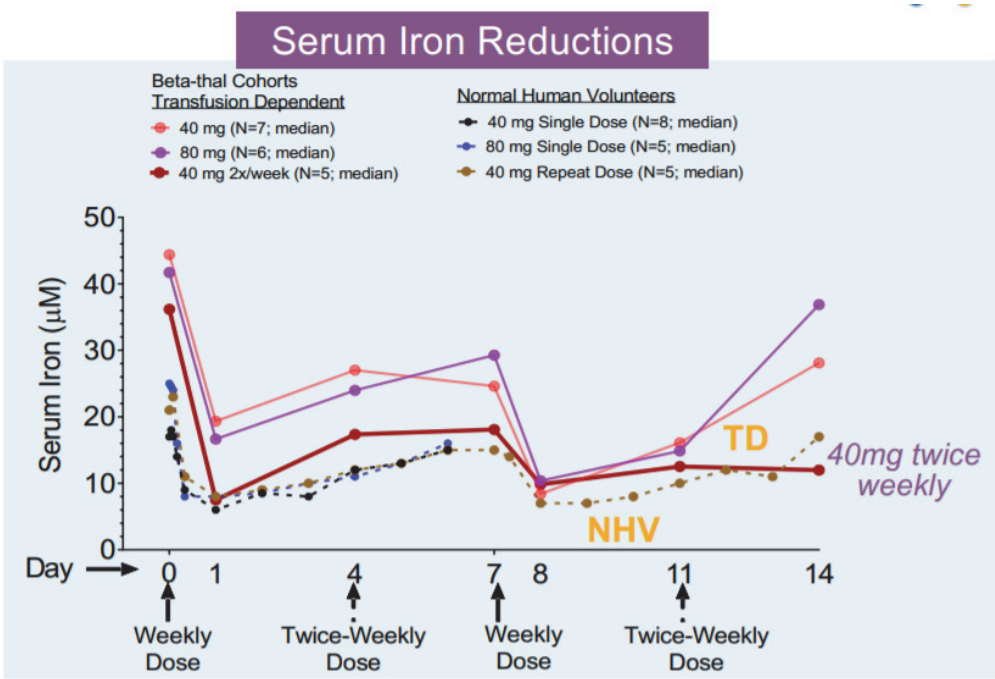
PTG-300 has received orphan drug designation from the FDA and EU regulatory authorities, and Fast Track designation from the FDA for the treatment of beta-thalassemia. Fast Track designation is an expedited review to facilitate development of investigational drugs which treat a serious or life-threatening condition and fill an unmet medical need. In 2018, we successfully filed an IND for PTG-300 in the United States and related clinical trial applications outside the United States.

In the first quarter of 2019, we began dosing patients in a global Phase 2 study of PTG-300 in beta-thalassemia called TRANSCEND. The study is a single-arm, open label, MAD design that evaluates safety, POC and dose finding in adolescent and adult patients with anemia associated with NTD or TD beta-thalassemia. NTD patients receive 12 weeks treatment with PTG-300 in escalating dose cohorts. The primary efficacy endpoint in NTD patients is a change in hemoglobin from baseline. TD patients receive 16 weeks treatment with PTG-300 in escalating dose cohorts. The primary efficacy endpoint in TD patients is a change in transfusion burden from baseline. The primary objectives of this study are to evaluate the safety, tolerability and preliminary efficacy of PTG-300 and identify an appropriate starting dose and titration regimen for registration studies.

Previously, we reported preliminary results from the Phase 2 study. Dose-related drug exposure reductions from baseline TSAT and serum iron levels were observed (Figure 2), with significant reductions at the 40 mg and 80 mg weekly doses and significant and sustained reductions at the 40 mg twice weekly doses.

Figure 2: PTG-300 Reduces TSAT and Serum Iron Levels – TD Beta-thalassemia Patients and Normal Human Volunteers ("NHV")





The dose-related pharmacodynamic responses in TSAT and serum iron levels observed in this preliminary analysis provide the first evidence of the effects of PTG-300 in patients with beta-thalassemia. These early results suggest the potential of finding an appropriate dose of PTG-300 for continued development in the treatment of beta-thalassemia. While we have observed clinical responders in the study based on the pre-specified criteria of reductions in transfusion burden, continued evaluation at higher doses will be required to evaluate the rate and durability of these

effects in order to reach definitive conclusions. We will continue further study with additional dose regimens and longer follow-up and expect to report topline results in 2020.

PTG-300 was well-tolerated and systemic adverse events were mild to moderate in severity and were typical of patients with beta-thalassemia. These events were not dose-related and did not prevent dose escalation. There was one serious drug-related adverse event of vomiting and confusion, and the most frequent treatment emergent adverse event observed was injection site erythema in 5 out of 39 patients (12.8%).

In the fourth quarter of 2019, we initiated a Phase 2 study of PTG-300 in PV designed to evaluate safety and preliminary efficacy in patients requiring phlebotomy. The Phase 2 study in PV is expected to enroll approximately 30 patients and consists of a 16-week open-label dose finding stage every 4 weeks from 10 mg to 80 mg and a 12-week maintenance period at doses which generate desired hematocrit levels, followed by a 12-week randomized and blinded withdrawal stage. The study has an open-label extension for up to one year to monitor long term safety and benefits of the drug. The endpoints of this clinical POC study include measurement of blood parameters (hematocrit and hemoglobin levels), reductions or delay in phlebotomy requirements, and improvements in quality-of-life symptoms.

In January 2020, we initiated a Phase 2 study of PTG-300 in HH. This study is an open label, multicenter study designed to evaluate the effects of PTG-300 in approximately 30 adult patients over 24 weeks of treatment. Guidelines for HH focus on controlling TSAT and ferritin to prevent long-term complications. Given the TSAT reductions from PTG-300 observed to date in both healthy volunteers and beta-thalassemia patients, as well as regulation of organ iron content in a mouse model of HH, we believe that a significant reduction in phlebotomy may be possible with PTG-300. The endpoints of this POC study include change in TSAT and serum iron levels, reductions in phlebotomy requirements and an assessment of participant-reported outcomes.

We expect to initiate an IST of PTG-300 in MDS in the first half of 2020.

Assuming PTG-300 shows clinical efficacy in one or more of the above indications, we intend to select our first indication in 2020 for a potential pivotal study to begin in 2021.

OVERVIEW OF INFLAMMATORY BOWEL DISEASE

IBD is a group of chronic autoimmune and inflammatory conditions of the colon and small intestine, consisting primarily of UC and CD. In UC, inflammation may be limited to part of the colon or extend through its entirety. UC is primarily characterized by ulceration of the intestinal surface, accompanied by rectal bleeding and frequent, urgent bowel movements. CD occurs anywhere along the GI tract, commonly affecting the small intestine and the proximal large intestine. CD complications may include strictures and fistula, which penetrate all layers of the intestine. UC is usually diagnosed earlier than CD due to bleeding symptoms. Patients with CD may initially present with abdominal pain, fatigue and anorexia, which can be misdiagnosed. Both diseases' peak diagnosis years are in young adulthood and are found about equally in both males and females. Management is lifelong and affects school attendance, graduation rates, childbearing and work productivity. IBD prevalence is increasing worldwide and is correlated with the adoption of western diets and lifestyle, as well as genetic factors (5 to 20% of affected patients have a first degree relative with the disease).

Market Overview

According to the Crohn's & Colitis Foundation of America, there are more than 1.6 million IBD patients in the United States alone, 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, and there may be as many as 80,000 children in the United States with IBD. GlobalData estimates that the UC market was approximately $5.3 billion across seven major markets: United States, France, Germany, Italy, Spain, United Kingdom and Japan. This is expected to increase at a compound annual growth rate of approximately 2.5% to $6.8 billion by 2026. In 2017, GlobalData estimated that the CD market reached approximately $9.6 billion across those same seven major markets and is expected to grow approximately 3.7% per year to $13.8 billion by 2026.

Johnson & Johnson global sales of Stelara® (approved for psoriasis, psoriatic arthritis, moderate-to-severe CD and UC) exceeded $5.0 billion in 2018. Takeda Pharmaceuticals sales of Entyvio® for IBD reached approximately $3.0 billion in 2019.

Current Standard of Care in IBD

In recent years, treatment of IBD has evolved from a focus on successful symptom management to an emphasis on modifying the underlying disease to achieve long-term remission. While available treatments exist for moderate-to-severe IBD, there continues to be a significant medical need for novel, efficacious, safe and convenient treatments. New technologies and outcome measures have been developed to improve staging definitions and assessments of treatment benefit. Nonetheless, halting or reversing IBD progression has not yet been achieved with any single agent therapy, and attaining and maintaining long-term remission in most patients remains a significant unmet medical need. Across therapeutic classes, 15% to 31% rates of clinical remission represent the current ceiling in patients with moderate-to-severely active disease.

Biosimilar infliximab and other tumor necrosis factor ("TNF") inhibitors are the first line standard of care in moderate-to-severe IBD. Anti-TNFs bind to and neutralize a central pro-inflammatory cytokine in the gut via systemic immunosuppression. As a result, they can be associated with infection and malignancy risk. Although the magnitude of these risks is relatively low, they are significant for the young IBD population who must continue on lifelong treatment. In addition, more than 10% of patients treated with anti-TNF agents lose response with each year of treatment. In 2014, a novel anti-trafficking mechanism launched with vedolizumab (Entyvio®), which blocks migration of leukocytes into the gut via α4β7 integrins. This mechanism remains the only true "gut selective" approach in the IBD market today, although formulation technologies can limit systemic exposure from orally delivered agents. Entyvio® has shown an excellent safety profile, although it requires intravenous administration. Entyvio® was followed by the launch of ustekinumab (Stelara®) in CD in 2016, which blocks inflammation produced through the Interleukin 12 ("IL-12") and Interleukin 23 ("IL-23") pathways, and tofacitinib (Xeljanz®), an orally delivered pan-Janus kinase (JAK) inhibitor approved in UC.

A head-to-head trial called VARSITY comparing the long-term safety and efficacy of an anti-integrin and anti-TNFs has been completed. Entyvio® demonstrated superior rates of clinical remission and endoscopic improvement compared with Humira, the market leader in the TNF inhibitor class. The first formal combination trials in IBD were initiated in the last year, adding new mechanisms such as integrin inhibitors or IL-23 inhibitors to anti-TNFs. Most IBD experts now believe that combining treatment classes with additive or synergistic mechanisms of action will be required to attain the disease-modifying effects and lasting remissions in a larger group of patients documented in other areas of immunology, such as psoriasis or rheumatoid arthritis.

We believe the development of new, potent and targeted orally delivered therapies for IBD may offer safer and more effective treatment options, alone or in combination, for moderate-to-severe IBD patients. In addition, many clinicians continue to advocate for earlier introduction of targeted therapeutics in mild-to-moderate IBD in order to prevent disease progression and irreversible gastrointestinal damage. Our orally delivered, GI-restricted, peptide drugs PTG-200 and PN-943 work on the same specific validated targets as FDA-approved injectable antibodies and have the potential to offer improved safety and compliance and to minimize the risk of immunogenicity associated with antibodies. We believe that our product candidates, if approved, have the potential to be used more broadly, including treatment of mild-to-moderate IBD.

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

For the IBD targets of interest, the size and nature of our peptides are carefully selected and modified so as to acquire the desired potency and specificity, and also to largely restrict their presence to the GI tissue compartment when administered orally. These features translate to orally delivered, 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 and 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 anti-drug antibodies 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 with the potential for improved efficacy.

- *Cost-effective and less complex manufacturing*. Because of their size and stability, we believe that our orally delivered, 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 orally delivered, 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, payors, and physicians.

PTG-200: AN ORALLY DELIVERED IL-23R ANTAGONIST

PTG-200, an orally delivered, gut-restricted IL-23R specific antagonist for the treatment of IBD, was discovered through our peptide technology platform. 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 IL-23R with PTG-200 in the GI tissue compartment, we hope to improve disease symptoms and reduce bowel wall damage while potentially minimizing the risk of systemic side effects due to its GI-restricted nature.

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 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 local 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 orally delivered, GI-restricted nature of PTG-200 may allow PTG-200 to be a potent inhibitor of the IL-23 pathway for the treatment of IBD. By targeting IL-23R with our orally delivered GI-restricted IL-23R antagonist PTG-200, we believe PTG-200 may 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 with the potential for concomitant efficacy benefits.

PTG-200's Phase 1 Clinical Study

We completed a Phase 1 clinical trial of PTG-200 in Australia during the fourth quarter of 2018. The Phase 1 study was a randomized, double-blind, placebo-controlled, SAD and MAD-escalation trial in 80 normal healthy volunteers. The primary endpoint was safety and tolerability. Secondary endpoints included the identification of the maximally tolerated dose and the evaluation of pharmacokinetic parameters.

Results of the Phase 1 study demonstrated that administration of PTG-200 was well-tolerated. No serious adverse events or dose-limiting toxicities were observed. The pharmacokinetic and pharmacodynamic parameters were consistent with the GI-restricted design of PTG-200.

PTG-200's Clinical Development Plan

We have a worldwide license and collaboration agreement with Janssen, to co-develop and co-detail PTG-200 and any second-generation compounds for all indications, including IBD. The agreement was amended in May 2019 to expand the collaboration by supporting efforts towards second-generation IL-23R antagonists, triggering a $25.0 million milestone payment to the Company. In January 2020, we announced the identification and nomination of an orally delivered, gut-restricted IL-23R antagonist peptide as a second-generation development candidate under our license and collaboration agreement with Janssen, advancing the collaboration and triggering a $5.0 million milestone payment to us. 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. Janssen submitted an IND for PTG-200 in CD during the second quarter of 2019, which took effect in July 2019.

In collaboration with Janssen, we initiated a Phase 2 clinical study in CD called PRISM in the fourth quarter of 2019. The global, randomized, double blind, placebo-controlled, Phase 2 study is evaluating the efficacy of oral administration of PTG-200 in 90 patients with moderate-to-severe CD. The study will assess the effect of twice-daily dosing of PTG-200 on change from baseline in Crohn's Disease Activity Index score at week 12 as the primary endpoint. The study will also assess change from baseline in simple endoscopic score for CD rates of clinical response and remission, endoscopic response and remission, and patient-reported outcome-2 remission. Results from this Phase 2 study in CD are expected in 2021.

PN-943: AN ORALLY DELIVERED α4β7 INTEGRIN ANTAGONIST

PN-943, an orally delivered, gut-restricted α4β7 specific integrin antagonist, was discovered through our peptide technology platform and is being developed initially for patients with moderate-to-severe UC. α4β7 integrin is considered to be one of the most GI-specific biological targets for IBD due to its binding to MAdCAM-1, an extracellular protein that resides mostly in the GI vasculature. PN-943 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. We believe that we can leverage the development and regulatory path of Entyvio® and other approved antibody drugs for IBD to help inform the design of our clinical development studies.

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 protein-protein interactions ("PPI") between the α4β7 integrin and its corresponding ligand, MAdCAM-1, which is primarily expressed in the GI tissue compartment. Hence, the binding of α4β7 to MAdCAM-1 can be categorized as a GI-specific interaction and has been identified as an IBD-specific targeted therapeutic approach. By blocking the binding of α4β7 integrin to MAdCAM-1, PN-943 may prevent T cells from entering the GI tissue compartment, thereby reducing the inflammation that leads to the clinical manifestations and long-term implications of UC.

α4β7 for IBD is targeted by the FDA-approved drug Entyvio®, which has demonstrated safety and efficacy in patients with moderate-to-severe UC and CD. Since PN-943 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 2 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.

PN-943 Pre-Clinical Proof-of-Concept Studies

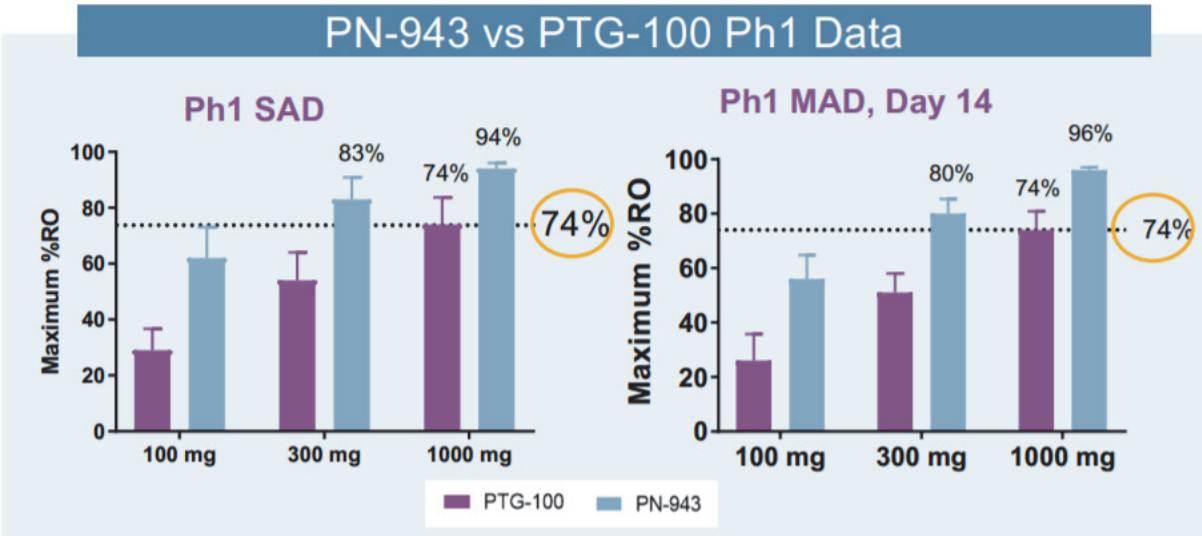
We have completed extensive pre-clinical studies of PN-943 in which we established pharmacodynamic target engagement POC, including effects on receptor occupancy, T cell trafficking and mucosal healing in rodents and monkeys. Based on pre-clinical data, we believe that PN-943 may be a more potent α4β7 integrin antagonist compound than PTG-100 without sacrificing its other positive attributes, such as selectivity and tolerability. PTG-100 is our first generation α4β7 inhibitor that shares the same α4β7 integrin target as Entyvio® for the treatment of moderate-to-severe UC and CD. We completed extensive pre-clinical studies of PTG-100 in which we established pharmacological POC and completed a Phase 1 clinical trial in Australia in 2016.

PN-943's Phase 1 Clinical Trial Overview

We completed a Phase 1 randomized, double-blind, placebo-controlled clinical trial of PN-943 in normal healthy male volunteers in Australia in 2019. The Phase 1 SAD and MAD components were conducted with a solution-based liquid formulation. In addition to determining the safety and tolerability and pharmacokinetics of PN-943, the SAD and MAD components of the trial evaluated PD-based POC through the assessment of α4β7 receptor occupancy and α4β7 target expression that indicate target engagement on peripheral blood memory T cells similar to what was done in the pre-clinical studies and in the Phase 1 trial with PTG-100. In the clinical trial, dose escalation proceeded from 100 mg up to 1,400 mg for the SAD portion and 1,000 mg for the MAD portion.

We reported results of the SAD part of the study during the second quarter of 2019 and the MAD part of the study during the third quarter of 2019. The pharmacodynamic results of target engagement were supportive of the three-fold higher potency of PN-943 as compared to PTG-100 and saturation at 1000 mg (Figure 3). This is consistent with data from pre-clinical studies and confirmed by this Phase 1 pharmacodynamic data. We believe this links PN-943 to greater probability of success in a Phase 2 trial based on signs of clinical efficacy of PTG-100 in the Phase 2 PROPEL trial in US patients. The administration of PN-943 was well-tolerated.

Figure 3: PN-943 vs. PTG-100: Dose Related and Saturable Effect on Blood % Receptor Occupancy ("RO")



PN-943 Clinical Development Plan

We filed an IND for PN-943 that took effect in January 2020. We expect to initiate a Phase 2 POC study of PN-943 in UC in the second quarter of 2020.

OUR PEPTIDE TECHNOLOGY PLATFORM

Our proprietary technology platform is purposefully built to exploit the advantages of constrained peptides, which are smaller than antibody-based drugs and may be delivered orally but are big enough to bind and block the difficult targets that antibodies bind and modulate. The platform has been successfully applied to a diverse set of biological targets that has led to several pre-clinical and clinical stage peptide-based new chemical entities, including our clinical stage product candidates, 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, stability assays, medicinal chemistry, biomarker, formulations, and *in vivo* pharmacology approaches. We apply this platform to the discovery and development of constrained peptides to develop new drug candidates.

The platform is used to develop potential drug candidates (agonists and antagonists): (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. The scaffolds identified 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 PTG-300, hit discovery and optimization relied exclusively on medicinal chemistry, with no phage display, to develop potent and selective injectable candidates with enhanced stability and exposure in blood. For injectable products, stability in blood is determined using *in vitro* assay techniques to identify chemical and biological sites of degradation, which are then optimized whilst maintaining potency and selectivity. Conjugation strategies are used to optimize the exposure of the injected peptide. For PN-943 and PTG-200, phage display is tightly coupled to medicinal chemistry and oral stability techniques to develop potent,

selective and orally delivered molecules that are GI-restricted. Oral stability is profiled in a series of *in vitro* and *ex vivo* assays that portray the chemical and metabolic barriers a peptide will encounter as it transits the GI tract. These metabolically labile spots in the peptides are optimized using medicinal chemistry-based approaches to engineer oral stability whilst maintaining selectivity and potency. Various *in vivo* pharmacology tools are then used to quantify peptide exposure in relevant GI organs and tissues. This data can be used to optimize required GI exposure over the required time frame to achieve *in vivo* efficacy. This is complemented by formulation studies to enhance GI exposure. Finally, various biomarkers are also developed to correlate exposure with efficacy to guide candidate selection, dose selection and provide preliminary proof-of-concept of target engagement in clinical trials.

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, 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, macrocyles and peptidomimetics, 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 for the clinical development, manufacture and potential commercialization of PTG-200 and any second-generation compounds worldwide for the treatment of CD and UC (the "Janssen License and Collaboration Agreement"). The Janssen License and Collaboration Agreement became effective on July 13, 2017 and was subsequently amended effective May 2019 (the "First Amendment"). The First Amendment expands the original collaboration by supporting efforts towards research and development of second-generation IL-23R antagonists. During the third quarter of 2017, we received a non-refundable, upfront cash payment of $50.0 million from Janssen. During the second quarter of 2019, we received a non-refundable cash payment of $25.0 million upon execution of the First Amendment. During the first quarter of 2020, we received a milestone payment of $5.0 million triggered by the identification and nomination of a second-generation development candidate. 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 disulfide-rich peptides to discover a hepcidin mimetic. We amended this agreement on February 28, 2014, at which point Protagonist assumed responsibility for the development program. 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.

We believe our principal competition in the treatment of chronic iron overload disorders such as beta-thalassemia will be luspatercept (Acceleron/Celgene-BMS) and mitapivat (Agios). Although gene therapy is potentially curative for

beta-thalassemia, we believe that Bluebird Bio's LentiGlobin will have limited application due to safety risks associated with its required "pre-conditioning" regimen, which is similar to allogeneic hematopoietic stem cell transplantation. Hematopoietic stem cell transplantation is infrequently utilized in beta-thalassemia due to its risk benefit profile in a younger patient population. Luspatercept and LentiGlobin have been approved in the United States and Europe, respectively, for TD beta-thalassemia, and are in Phase 3 development for beta-thalassemia, and mitapivat is in Phase 2 studies for beta-thalassemia. An IND for Luspatercept has been filed in the United States for thalassemia and MDS.

There are currently no approved orally delivered peptide-based α4β7 or IL-23R products for IBD. We believe our principal competition in the treatment of IBD will come from companies with injectable agents in the anti-integrin class that are or will be approved by 2028, including:

- Takeda's Vedolizumab (Entyvio®) IV and SC (IV approved, SC Phase 3);
- Roche's Etrolizumab SC (Phase 3); and
- Shire's SHP-647 SC (Phase 3; divested as part of the Takeda acquisition of Shire - buyer to be determined).

In addition, orally delivered agents with novel mechanisms of action are approved or in development and may be approved for UC and/or CD prior to the launch of PTG-200 and PN-943. These include JAK inhibitors, pan-JAK tofacitinib (Xeljanz) approved in UC and next-generation JAK1 inhibitors filgotinib and upadacitinib, as well as S1P inhibitors, ozanimod, amiselmod and etrasimod. The anti-IL-23 antibodies are also demonstrating positive data in IBD. Our clinical asset PTG-200 will compete as the only orally delivered IL-23R antagonist.

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 own or co-own 16 issued U.S. patents, over 20 granted ex-U.S. patents, and numerous U.S. and ex-U.S. patent applications related to our clinical assets. We 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. Specific patents and patent applications are directed to compositions of α*4*β7 integrin peptides, IL-23R antagonist peptides, and hepcidin and enkephalin mimetics peptides, as well as methods of synthesizing and using these peptides to treat inflammatory disorders. Applications are currently pending in the United States and other

major jurisdictions, including Australia, Canada, China, Japan, and Europe. We expect our patents and patent applications, if issued, and if the appropriate maintenance, renewal, annuity, or other governmental fees are paid, to expire from October 2033 to July 2039 (excluding possible patent term extensions).

Our objective is to continue to expand our portfolio of patents and patent applications in order to protect our clinical assets and related peptide-based drug technologies.

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. Some licensed patents are expired, and others are expected to expire before or by 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, 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 for pre-clinical and clinical studies and eventually for commercial supplies, 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. We expect third-party manufacturers to be capable of providing needed 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 for 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 our 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 current good manufacturing practices ("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.

Fast Track Designation

The FDA has various programs, including fast track designation, which are intended to expedite or simplify the process for the development and FDA review of drugs that are intended for the treatment of serious or life threatening diseases or conditions and demonstrate the potential to address unmet medical needs. The purpose of these programs is to provide important new drugs to patients earlier than under standard FDA review procedures. Under the fast track program, the sponsor of a new drug candidate may request that the FDA designate the drug candidate for a specific indication as a fast track drug concurrent with, or after, the filing of the IND for the drug candidate. To be eligible for a fast track designation, the FDA must determine, based on the request of a sponsor, that a product is intended to treat a serious or life threatening disease or condition and demonstrates the potential to address an unmet medical need. The FDA will determine that a product will fill an unmet medical need if it will provide a therapy where none exists or provide a therapy that may be potentially superior to existing therapy based on efficacy or safety factors. Fast track designation provides additional opportunities for interaction with the FDA's review team and may allow for rolling review of NDA components before the completed application is submitted, if the sponsor provides a schedule for the submission of the sections of the NDA, the FDA agrees to accept sections of the NDA and determines that the schedule is acceptable, and the sponsor pays any required user fees upon submission of the first section of the NDA. However, the FDA's time period goal for reviewing an application does not begin until the last section of the NDA is submitted. The FDA may decide to rescind the fast track designation if it determines that the qualifying criteria no longer apply.

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, and 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 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 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.

There remain 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, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the ACA-mandated "Cadillac" tax on high-cost employer-sponsored health coverage and the medical device tax and, effective January 1, 2021, also eliminates the health insurance tax. 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. On December 14, 2018, a Texas U.S. District Court Judge ruled that the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress as part of the Tax Act. Additionally, on December 18, 2019, the U.S. Court of Appeals for the 5th Circuit upheld the District Court ruling that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the ACA are invalid as well. It is unclear how this decision, future decisions, subsequent appeals, and other efforts to repeal and replace the ACA will impact the ACA and our business.

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 2029 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. 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 2021 includes a $135 billion allowance to support legislative proposals seeking to reduce drug prices, increase competition, lower out-of-pocket drug costs for patients, and increase patient access to lower-cost generic and biosimilar drugs. Further, the Trump administration released a "Blueprint" to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase drug manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products, and reduce the out of pocket costs of drug products paid by consumers. The Department of Health and Human Services, or HHS, has solicited feedback on some of these measures and, at the same, has implemented others under its existing authority. For example, in May 2019, CMS issued a final rule to allow Medicare Advantage plans the option to use step therapy for Part B drugs beginning January 1, 2020. This final rule codified CMS's policy change that was effective January 1, 2019. While some measures may require additional authorization 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 and, beginning in 2022, applicable manufacturers also will be required to report such information regarding payments and transfers of value provided, as well as ownership and investment interests held, during the previous year to physician assistants, nurse practitioners, clinical nurse specialists, certified nurse anesthetists and certified nurse-midwives.

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. In addition, certain states and local jurisdictions require the registration of pharmaceutical sales representatives.

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 significant administrative, civil and criminal penalties, damages, fines, 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. 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.

Employees

As of December 31, 2019, we had 73 full-time employees, 54 of whom were in research and development, of which three hold an M.D. and 20 hold Ph.D. degrees. The remaining 19 employees worked in finance, business development, human resources and administrative support, of which three 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 Clinical Development

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 early stage clinical trials of our pipeline candidates and conducting research to identify additional product candidates. We have not yet demonstrated an ability to generate product 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;
- 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 our collaboration agreements;
- competition from existing products as well as new products that may receive marketing approval;
- the entry of generic or biosimilar 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;
- 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, conduct clinical trials with good clinical practices ("GCP") and, if approved, for successful commercialization;
- our ability to maintain, expand and protect our intellectual property portfolio; 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 are heavily dependent on the success of our product candidates 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 registrational or pivotal clinical trials or are approved for commercial sale, and we may never 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 current product candidates and the development of other product candidates. We cannot be certain that our product candidates will receive regulatory approval or, if approved, be successfully commercialized. The research, testing, manufacturing, labeling, approval, sale, marketing and distribution of our product candidates will remain subject to extensive regulation by the U.S. Food and Drug Administration ("FDA") and other regulatory authorities in the United States and other countries. 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 approval by corresponding regulatory authorities. 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;
- Fast Track designation, which we have received for PTG-300 for the treatment of beta-thalassemia, may not lead to faster development or approval, and such designation may be revoked if we no longer meet the criteria for designation;
- 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; and

- 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.

Our product candidates will require additional research, clinical development, manufacturing activities, regulatory approval in multiple jurisdictions, securing sources of commercial manufacturing supply and partnering with a commercial organization. We cannot assure you that our clinical trials for our product candidates 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 would be expected to adversely affect our business and cause our stock price to fall. For example, the announcement of the premature discontinuation of the global Phase 2 clinical trial of PTG-100 for the treatment of moderate-to-severe UC in March 2018 due to the interim analysis meeting futility criteria on the primary endpoint of clinical remission (that was subsequently confirmed to be due to human error in endoscopy reads by the original vendor) significantly depressed our stock price.

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.

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. Any hypothesis formed from pre-clinical or early clinical observations for any of our product candidates may prove to be incorrect, and the data generated in animal models or observed in limited patient populations may be of limited value, and may not be applicable in clinical trials conducted under the controlled conditions required by applicable regulatory requirements.

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 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. 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. 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 and retaining 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. In addition, there are a significant number of global clinical trials in IBD and in hematologic disorders 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, such as the premature termination of our Phase 2 clinical trial of PTG-100 for the treatment of moderate-to-severe UC, may make it difficult or impossible to recruit and retain patients in other clinical trials of that same product candidate. Delays or failures in planned patient enrollment or retention may result in increased costs, program delays or both.

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, 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.

All of our peptide-based product candidates other than PTG-300, PTG-200 and PN-943 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 seek to discover, develop and commercialize a portfolio of new peptide-based product candidates in addition to PTG-300, PTG-200, and PN-943. 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.

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. 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, an independent data monitoring committee 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-200 and PN-943 have been 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.

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 mainly on the development of PTG-300 for treatment of certain rare blood disorders and the discovery and development of PTG-200, including any second-generation compounds, and PN-943, GI-restricted drugs that target the same biological pathways as currently marketed injectable antibody drugs for the treatment of IBD. As a result, we may forego or delay pursuit of opportunities with other product candidates or for other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. 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.

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, 2019, 2018 and 2017 was $77.2 million, $38.9 million and $37.0 million, respectively. As of December 31, 2019 and 2018, we had an accumulated deficit of $217.7 million and $140.5 million, respectively. 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 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 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 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. 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 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 any of our 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 and any second-generation compounds, 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, 2019, we had cash, cash equivalents and marketable securities of $133.0 million. Based upon our current operating plan and expected expenditures, we believe that our existing cash, cash equivalents, and marketable securities and proceeds from our debt facility will be sufficient to fund our operations for at least the next 12 months. However, 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 scope, progress, results and costs of drug discovery, clinical development, laboratory testing and clinical trials for our product candidates;
- the number of product candidates that we intend to develop using our technology platform;
- the costs, timing and outcome of any regulatory review of our product candidates;
- the timing and 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;
- the costs and timing of commercialization activities, including manufacturing, marketing, sales and distribution for any product candidates that receive marketing approval;

- Janssen's ability to successfully market and sell PTG-200 and any second-generation compounds upon regulatory approval and clearance, in the United States and other countries;

- 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 existing and additional personnel;

- our ability to establish and maintain collaborations on favorable terms, if at all, and the payment and achievement of the fees, milestone payments and royalties under those collaborations, including the Janssen License and Collaboration Agreement; and

- the emergence of competing technologies or other adverse market developments.

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. 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. To the extent that we raise additional capital through the sale of equity securities, including sales of common stock pursuant to our sales agreement with Jefferies LLC (the "Sales Agreement"), your ownership interest will be diluted, and the terms may include liquidation or other preferences that adversely affect your rights as a stockholder. If we issue common stock or securities convertible into common stock, our common stockholders would experience additional dilution and, as a result, our stock price may decline.

Covenants in our credit and security agreement restrict our business and operations in many ways and if we do not effectively manage our covenants, our financial conditions and results of operations could be adversely affected.

In October 2019, we entered into a credit and security agreement (the "Credit Agreement") pursuant to which we have borrowed $10.0 million to date and an additional $40.0 million is available, subject to specified availability periods and the satisfaction of certain conditions. All of our assets, except for intellectual property and certain other customary excluded property, are security for our borrowings under the Credit Agreement. The Credit Agreement contains customary affirmative and negative covenants, including, among other things, restrictions on indebtedness, liens, investments, mergers, dispositions, prepayment of other indebtedness and dividends and other distributions, any of which could restrict our business and operations, particularly our ability to respond to changes in our business or to take specified actions to take advantage of certain business opportunities that may be presented to us.

Our failure to comply with any of the covenants could result in a default under the Credit Agreement, which would permit the lenders to declare all or part of any outstanding borrowings to be immediately due and payable, or to refuse to permit additional borrowings under the loan and security agreement. If we are unable to repay those amounts, the lenders under the Credit Agreement could proceed against the collateral granted to them to secure that debt, which would seriously harm our business. In addition, before we borrow additional funds under the Credit Agreement, we must first satisfy ourselves that we will have access to existing and future alternate sources of capital, including cash flow

from our own operations, equity capital markets or debt capital markets in order to repay any principal borrowed, which we may be unable to do, in which case, our liquidity and ability to fund our operations may be substantially impaired.

Risks Related to Our Reliance on Third Parties

If Janssen does not elect to continue the development of PTG-200 or any second-generation compounds, our business and business prospects would be significantly harmed.

Under the terms of the Janssen License and Collaboration Agreement, Janssen may terminate the research program for second-generation compounds after an agreed upon period, and retains the right to terminate the Janssen License and Collaboration Agreement for convenience and without cause on written notice of a certain period. In addition, Janssen will generally retain control over the further clinical development of PTG-200 and the clinical development of second-generation compounds. Janssen's decisions with respect to such development will affect the timing and availability of potential future opt-in, milestone and royalty payments, if any. If the research program or the Janssen License and Collaboration agreement are terminated early, or if Janssen's development activities are terminated early or suspended for an extended period of time, or are otherwise unsuccessful, our business and business prospects would be materially adversely affected.

If there are any safety or efficacy results that cause the benefit-risk profile of PTG-200 or any second-generation compounds to become unacceptable, clinical development 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 or any second-generation compounds 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. If regulatory submissions requesting approval to market PTG-200 or any such second-generation compounds 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 treatment is unacceptable, and clinical development 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 or any second-generation compounds may not uncover all possible adverse events that patients may experience. We or Janssen may in the future observe or report dose-limiting or other safety issues in potential future clinical trials.

The occurrence of these events may cause Janssen to abandon its development of PTG-200 or any second-generation compounds 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 and any second-generation compounds.

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 or any second-generation compounds, 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 and any second-generation

compounds. 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.

We may not be successful in obtaining or maintaining development and commercialization collaborations, any collaboration arrangements we enter into in the future may not be successful, 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 active collaborations for any of our product candidates. Even if we are able to establish other collaboration arrangements, any such collaboration may not ultimately be successful, which could have a negative impact on our business, results of operations, financial condition and growth prospects. While we currently plan to enter into collaborations that are limited to certain identified territories, there can be no assurance that we would maintain significant rights or control of future development and commercialization of such product candidate. Accordingly, if we collaborate with a third party for development and commercialization of a product candidate, we may relinquish some or all of the control over the future success of that product candidate to the third party, and that partner may not devote sufficient resources to the development or commercialization of our product candidate or may otherwise fail in development or commercialization efforts, in which event the development and commercialization of the product candidate in the collaboration could be delayed or terminated and our business could be substantially harmed. In 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. 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.

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;

- 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;

- 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; 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.

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.

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. 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 cGMP and for Europe and other major regions, International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use ("ICH") guidelines, and we rely on contract manufacturers 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. As we proceed with the development and potential commercialization of our product candidates, 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 our product candidates could be materially adversely affected. Moreover, our contract manufacturers are the sole source of supply for our clinical product candidates. If we were to experience an unexpected loss of supply for any reason, whether as a result of manufacturing, supply or storage issues, natural disasters, pandemics 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 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.

Risks Related to Regulatory Approval

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 peptide-based product candidates. We are not permitted to market or promote any of our peptide-based product candidates before we receive regulatory approval from the FDA, the EMA or any other foreign regulatory authority, and we may never receive such regulatory approval for any of our peptide-based product candidates. The time required to obtain approval by the FDA and comparable foreign authorities is unpredictable, typically takes many years following the commencement of clinical trials and depends upon numerous factors. 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;
- 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.

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.

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 United States, including additional pre-clinical studies or clinical trials. In many countries outside the United States, a product candidate must be approved for reimbursement before it can be approved for sale in that country. 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. If we fail to comply with the regulatory requirements in international markets or to 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.

We may fail to obtain orphan drug designations from the FDA and/or EU 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.

PTG-300 has received orphan drug designation for the treatment of patients with beta-thalassemia from the FDA and EU. Despite this designation, we may be unable to maintain the benefits associated with orphan drug status, including market exclusivity. 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. In addition, while we may seek orphan drug designation for our product candidates, we may never receive such designations.

Risks Related to Commercialization of our Product Candidates

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 (as described below), which would require us to establish a U.S. sales team. 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.

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 an option, which, if PTG-200 and/or any second-generation compounds are 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 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. 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 and/or any second-generation compounds 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 and/or any second-generation compounds. In such event, commercialization 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.

Even if our 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 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 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, marketing and distribution efforts;
- the cost of treatment in relation to alternative treatments;
- 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 product candidates in addition to or in the place of current injectable therapies;
- 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.

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.

There remain 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. Since January 2017, the President has signed two Executive Orders and other directives designed to delay the implementation of 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. Additionally, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the ACA-mandated "Cadillac" tax on high-cost employer-sponsored health coverage and the medical device tax and, effective January 1, 2021, also eliminates the health insurance tax. Further, the Bipartisan Budget Act of 2018 (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." Congress may consider other legislation to repeal or replace other elements of the ACA. On December 14, 2018, a Texas U.S. District Court Judge ruled that the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress as part of the Tax Act. Additionally, on December 18, 2019, the U.S. Court of Appeals for the 5th Circuit upheld the District Court ruling that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the ACA are invalid as well. It is unclear how this decision, future decisions, subsequent appeals and other efforts to repeal and replace the ACA will impact the ACA and our business.

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 2029 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.

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 2021 includes a $135 billion allowance to support legislative proposals seeking to reduce drug prices, increase competition, lower out-of-pocket drug costs for patients and increase patient access to lower-cost generic and biosimilar drugs. Further, the current administration released a "Blueprint" to lower drug prices and reduce out-of-pocket costs of drugs that contains additional proposals to increase drug manufacturer competition, increase the negotiating power of certain federal health programs, incentivize manufacturers to lower the list price of their products and reduce the out-of-pocket costs of drug products paid by consumers. While some of the measures may require additional authorization 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. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our product candidates, if approved.

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

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

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

In some countries, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product candidate. In addition, there can be considerable pressure by governments and other stakeholders on prices and reimbursement levels. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after coverage and reimbursement have been obtained. 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.

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. 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 and intellectual property protections in foreign countries;
- trade-protection measures, import or export licensing requirements such as Export Administration Regulations promulgated by the U.S. 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;
- differing payor reimbursement regimes, governmental payors or patient self-pay systems and price controls;
- 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 U.S., more expensive.

If we are unable to anticipate and address these risks properly, our business and financial results will be harmed.

Our business could be adversely affected by the effects of health epidemics, including the recent coronavirus, or COVID-19, outbreak, in regions where we or third parties on which we rely have significant manufacturing and distribution facilities, concentrations of clinical trial sites or other business operations. We have clinical trial sites in countries that have been directly affected by COVID-19, and depend on outsourced manufacturing operations, including China, for various stages of our supply chain. In addition, if COVID-19 becomes a pandemic, it could materially affect our operations globally, including at our headquarters in the San Francisco Bay Area and at our clinical trial sites throughout the globe.

Our business could be adversely affected by health epidemics in regions where we have significant manufacturing and distribution facilities, concentrations of clinical trial sites or other business operations.

If the recent coronavirus, or COVID-19, outbreak continues to spread, we may need to limit operations or implement limitations, including work from home policies. There is a risk that some countries or regions may be less effective at containing COVID-19, or it may be more difficult to contain if the outbreak reaches a larger population or broader geography, in which case the risks described herein could be elevated significantly.

In particular, some of our suppliers of certain materials, including certain critical active pharmaceutical ingredients, used in the production of our drug products are located in China, and possibly other affected areas. While many of these materials may be obtained by more than one supplier, including suppliers outside of China, port closures, country lockdowns, and other restrictions resulting from the COVID-19 outbreak in a region may disrupt our supply chain or limit our ability to obtain sufficient materials for our drug products. While we are closely monitoring developments and are implementing and evaluating new mitigation strategies, the full impact of this outbreak is uncertain at this time and any prolonged disruption to our manufacturers and distributors could significantly disrupt our supply chain and could have a material adverse effect on our development plans and business.

In addition, our clinical trials may be affected by the COVID-19 outbreak. Site initiation and patient enrollment may be delayed or disrupted due to prioritization of hospital and medical resources toward the COVID-19 outbreak or inability to access hospital and other clinical sites. Further, site initiation and patient enrollment may be delayed due to difficulties related to clinical site investigators, clinical site staff and patients who may be reluctant to travel to medical sites to comply with clinical trial protocols or be monitored. If COVID-19 becomes a pandemic, it may delay enrollment in our global clinical trials, some patients may not be able to comply with clinical trial protocols if quarantines impede patient movement or interrupt healthcare services, and we may be unable to obtain data from blood samples or other required medical procedures.

The ultimate impact of the COVID-19 outbreak or a similar health epidemic is highly uncertain and subject to change. We do not yet know the full extent of potential delays or impacts on our business, our supply chain, clinical trials, healthcare systems or the global economy as a whole. However, these effects could have a material impact on our operations, and, therefore, we will continue to monitor the COVID-19 situation closely and implement risk mitigation as needed.

Risks Related to Our Business and Industry

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. 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, there would be a material adverse impact on the future prospects for our product candidates and business.

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 competitor products;
- 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.

If we fail to comply with state and federal healthcare regulatory laws, we could face substantial penalties, damages, fines, disgorgement, integrity oversight and reporting obligations, 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;
- the federal false claims laws, including the False Claims Act;
- the federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA");
- 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;
- the federal Physician Payments Sunshine Act; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws.

Further, the ACA, among other things, amended the intent requirements of the federal Anti-Kickback Statute and certain criminal statutes governing healthcare fraud. 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. Federal and state enforcement bodies have continued to increase 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. 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.

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

As of December 31, 2019, we had 73 full-time employees, including 54 employees engaged in research and development. As our development and commercialization plans and strategies develop and we continue to 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; and

- improving our managerial, development, operational and financial systems and controls.

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. 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, and 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. 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, (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. 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.

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"). 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, but also have their own methods and approval process. Therefore, coverage and reimbursement can differ significantly from payor to payor. 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.

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 product 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. 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. 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. 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.

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. For example, our granted U.S. patents covering PN-943 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 U.S. Patent and Trademark Office (the "PTO"), this increase can be reduced or eliminated based on certain delays caused by the patent applicant during patent prosecution. 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.

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 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. 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.

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. Also, 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. 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.

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. 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.

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. 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. 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. 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. 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.

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 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 stockholders. 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.

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. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the PTO, or made a misleading statement, during prosecution. Third parties may also raise similar claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, inter partes review, post grant review, and equivalent proceedings in foreign jurisdictions, such as opposition or derivation proceedings. Such proceedings could result in revocation or amendment to our patents in such a way that they no longer cover and protect our product candidates or technologies. The outcome following legal assertions of invalidity and unenforceability is

unpredictable. With respect to the validity of our patents, for example, we cannot be certain that there is no invalidating prior art of which we, our patent counsel, and the patent examiner were unaware 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 IL-23R, 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. 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.

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, are unpredictable and generally expensive and time-consuming and, even if resolved in our favor, are 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. 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.

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. 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 our industry expands 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 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. In the event of a successful claim of infringement against us, we may have to pay substantial damages, limit our uses, pay royalties or redesign our infringing product candidates, which may be impossible or require substantial

time and monetary expenditure. We may choose to seek, or may be required to seek, a license from the third-party patent holder and would most likely be required to pay license fees or royalties or both, each of which could be substantial. These licenses may not be available on commercially reasonable terms, however, or at all. Even if we were able to obtain a license, the rights we obtain may be nonexclusive, which would provide our competitors access to the same intellectual property rights upon which we are forced to rely. Furthermore, even in the absence of litigation, we may need to obtain licenses from third parties to advance our research or allow commercialization of our product candidates, and we have done so from time to time. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In such an event, we would be unable to further practice our technologies or develop and commercialize any of our product candidates at issue, which could harm our business significantly.

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

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

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

We may not be successful in obtaining or maintaining necessary rights to protect 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 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. 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.

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 patents 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 or co-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 co-own 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, consultants or independent contractors 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. 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. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership.

Some of our intellectual property was generated through government funded programs and thus may be subject to federal regulations such as "march-in" rights, certain reporting requirements and a preference for U.S.-based companies. Compliance with such regulations may limit our exclusive rights and limit our ability to contract with non-U.S. manufacturers.

Some of our intellectual property rights were generated through the use of U.S. government funding and are therefore subject to certain federal regulations. As a result, the U.S. government may have certain rights to intellectual property embodied in our current or future product candidates pursuant to the Bayh-Dole Act of 1980, or Bayh-Dole Act, and implementing regulations. These U.S. government rights in certain inventions developed under a government-funded program include a non-exclusive, non-transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the U.S. government has the right to require us or our licensors to grant exclusive, partially exclusive, or non-exclusive licenses to any of these inventions to a third party if it determines that: (i) adequate steps have not been taken to commercialize the invention; (ii) government action is necessary to meet public health or safety needs; or (iii) government action is necessary to meet requirements for public use under federal regulations (also referred to as "march-in rights"). The U.S. government also has the right to take title to these inventions if we, or the applicable licensor, fail to disclose the invention to the government and fail to file an application to register the intellectual property within specified time limits. These time limits have recently been changed by regulation and may change in the future. Intellectual property generated under a government funded program is also subject to certain reporting requirements, compliance with which may require us or the applicable licensor to expend substantial resources. In addition, the U.S. government requires that any products embodying the subject invention or produced through the use of the subject invention be manufactured substantially in the United States. The manufacturing preference

requirement can be waived if the owner of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the United States or that under the circumstances domestic manufacture is not commercially feasible. This preference for U.S. manufacturers may limit our ability to contract with non-U.S. product manufacturers for products covered by such intellectual property. To the extent any of our current or future intellectual property is generated through the use of U.S. government funding, the provisions of the Bayh-Dole Act may similarly apply.

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.

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.

Our stock price has fluctuated in the past and is likely to be volatile in the future. The stock market in general and the market for biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, investors may experience losses on their investment in our common stock. 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:

- the success of competitive products or technologies;
- regulatory actions with respect to our product candidates or our competitors' products and product candidates;
- actual or anticipated results in our clinical trials or those of our competitors;
- regulatory or legal developments in the United States and other countries;
- disputes or developments concerning patent applications or other proprietary rights;
- the level of expenses related to any of our product candidates or clinical development programs;
- adverse regulatory decisions;
- 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;
- variations in our financial results or those of companies that are perceived to be similar to us;
- actual or anticipated variations in quarterly operating results;
- announcement or expectation of additional financing efforts;
- sales of our common stock by us or our stockholders in the future;
- the trading volume of our common stock;
- actual or anticipated changes in estimates as to financial results, timelines or recommendations by analysts;
- changes in the structure of healthcare payment systems;
- conditions or trends in the biotechnology and biopharmaceutical industries; and
- general political and economic conditions.

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. 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 and current beneficial owners of 5% or more of our common stock, in the aggregate, beneficially own a significant percentage of our outstanding common stock. These persons, acting together, will be able to significantly influence all matters requiring stockholder approval, including the election and removal of directors and any merger or other significant corporate transactions. The interests of this group of stockholders may not coincide with the interests of other stockholders.

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, 2019, we had a total of 27,217,649 shares of common stock outstanding, 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 sales of common stock pursuant to our Sales Agreement. 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.

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 for as long as we continue to be an "emerging growth company," we intend to take advantage of exemptions from various reporting requirements applicable to other public companies but not to "emerging growth companies," including, but not limited to, not being required to comply with the auditor attestation requirements of Section 404, reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and shareholder 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 $700.0 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. If some investors find our common stock less attractive as a result of our choices to reduce disclosure, there may be a less active trading market for our common stock, and our stock price may be more volatile.

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 are 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. This assessment needs 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". 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.

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

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 any 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.

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, 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 are 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.

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.

Provisions in our corporate charter documents and under Delaware law may prevent or frustrate attempts by our stockholders to change our management or hinder efforts to acquire a controlling interest in us, and the market price of our common stock may be lower as a result.

There are provisions in our certificate of incorporation and bylaws that may make it difficult for a third party to acquire, or attempt to acquire, control of our company, even if a change in control was considered favorable by our stockholders. Our charter documents also contain other provisions that could have an anti-takeover effect, such as:

- 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;
- our stockholders may not act by written consent or call special stockholders' meetings;
- our certificate of incorporation does not provide for cumulative voting in the election of directors;
- 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; and
- our board of directors may issue, without stockholder approval, shares of undesignated preferred stock.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which prohibit a person who owns 15% or more of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner. Any provision in our certificate of incorporation or our bylaws or Delaware law that has the effect of delaying or deterring a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock, and could also affect the price that some investors are willing to pay for our common stock.

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

In December 2017, 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 rates; limitation of the tax deduction for interest expense 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. 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, 2019, we had federal net operating loss carryforwards of approximately $164.1 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.

We may have additional tax liabilities.

Our effective income tax rate in the future could be adversely affected by a number of factors, including: interpretations of existing tax laws, changes in tax laws and rates, future levels of research and development expenditures, changes in the valuation of deferred tax assets and liabilities, our ability to use some or all of our accumulated net operating losses, changes in accounting standards and other items. The impact of our income tax provision resulting from these items may be significant and could have a negative impact on our net operating results. We are also subject to non-income based taxes, such as payroll, sales, use, property, and goods and services taxes in the United States. We may have additional exposure to non-income based tax liabilities.

We are regularly subject to audits by tax authorities in the jurisdictions in which we conduct business. Although we believe our tax positions are reasonable, the final outcome of tax audits and related litigation could be materially different than that reflected in our historical income tax provisions and accruals, and we could be subject to assessments of additional taxes and/or substantial fines or penalties. The resolution of any audits or litigation could have an adverse effect on our financial position and results of operations. We and our subsidiary are engaged in intercompany transactions, the terms and conditions of which may be scrutinized by tax authorities, which could result in additional tax and/or penalties becoming due.

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 be involved in legal proceedings arising in the ordinary course of business.

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.

Stockholders

As of the close of business on February 28, 2020, there were 2 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.

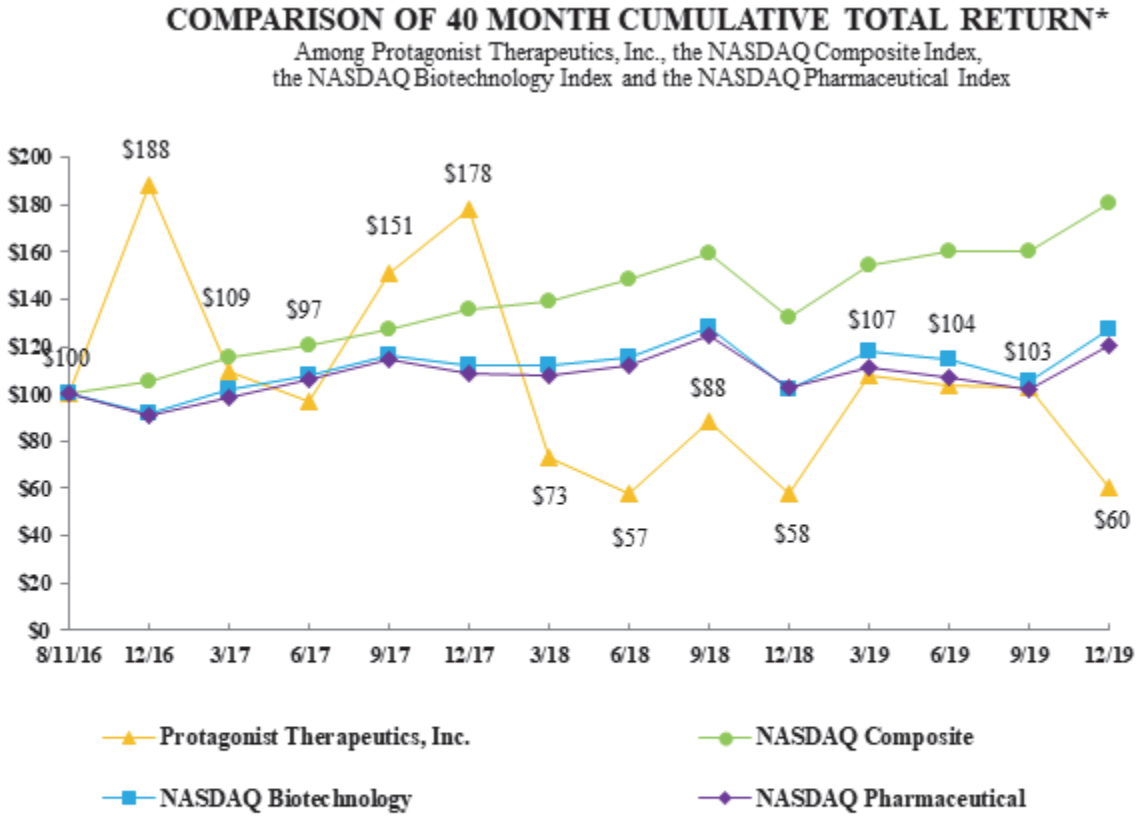
Dividend Policy

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 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, 2019.



**The stock price performance included in the draft is not necessarily indicative of future stock price performance.*

Sale of Unregistered Securities

None.

Repurchases of Shares or of Company Equity Securities

None.

Item 6. Selected Financial Data

The following selected consolidated statement of operations data for the years ended December 31, 2019, 2018, and 2017 and the consolidated balance sheet data as of December 31, 2019 and 2018 are derived from our audited consolidated financial statements that are included elsewhere in this report. The selected consolidated statement of operations data for the years ended December 31, 2016 and 2015 and the consolidated balance sheet data at December 31, 2017, 2016 and 2015 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,				
	2019	2018	2017	2016 (1)	2015
	(In thousands, except for share and per share data)				
Consolidated Statement of Operations Data:					
License and collaboration revenue - related party	$ 231	$ 30,925	$ 20,063	$ —	$ —
Operating expenses:					
Research and development	65,003	59,497	46,181	25,705	11,831
General and administrative	15,749	13,697	11,779	6,961	2,963
Total operating expenses	80,752	73,194	57,960	32,666	14,794
Loss from operations	(80,521)	(42,269)	(37,897)	(32,666)	(14,794)
Interest income	2,813	2,566	948	242	19
Interest expense	(169)	—	—	—	—
Other expense, net	(1)	(20)	(8)	(34)	—
Change in fair value of redeemable convertible preferred stock tranche and warrant liabilities [1]	—	—	—	(4,719)	(83)
Loss before income tax benefit	(77,878)	(39,723)	(36,957)	(37,177)	(14,858)
Income tax benefit	691	799	—	—	—
Net loss	$ (77,187)	$ (38,924)	$ (36,957)	$ (37,177)	$ (14,858)
Net loss attributable to common stockholders [2]	$ (77,187)	$ (38,924)	$ (36,957)	$ (37,735)	$ (14,933)
Net loss per share attributable to common stockholders, basic and diluted	$ (2.98)	$ (1.74)	$ (2.09)	$ (5.80)	$ (59.32)
Weighted-average shares used to compute net loss per share attributable to common stockholders, basic and diluted	25,894,024	22,364,515	17,694,505	6,501,796	251,717

[1] The 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. The change of $4.7 million for the year ended December 31, 2016 was 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.

[2] Net loss attributable to common stockholders is calculated by adjusting our net loss for the accretion of redeemable convertible preferred common stock, if any.

	December 31,				
	2019	2018	2017	2016	2015
			(In thousands)		
Consolidated Balance Sheet Data:					
Cash, cash equivalents and marketable securities	$ 133,017	$ 128,853	$ 155,459	$ 87,749	$ 11,923
Working capital	109,905	111,345	108,392	76,809	11,080
Total assets	154,917	139,472	163,734	93,990	14,845
Deferred revenue - related party	41,530	8,223	31,752	—	—
Long-term debt	9,794	—	—	—	—
Redeemable convertible preferred stock tranche liability [1]	—	—	—	—	1,643
Redeemable convertible preferred stock warrant liability [2]	—	—	—	—	480
Redeemable convertible preferred stock [3]	—	—	—	—	36,996
Accumulated deficit	(217,661)	(140,474)	(101,550)	(64,593)	(27,416)
Total stockholders' equity (deficit)	79,964	112,515	120,632	87,555	(27,400)

(1) We determined that our obligation to issue additional shares of our redeemable convertible preferred stock represented 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.

(2) We accounted for freestanding warrants to purchase shares of our 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 were recorded in the consolidated statements of operations. We 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 was required.

(3) Following the closing of our initial public offering in August 2016, all outstanding shares of redeemable preferred stock converted to common stock and the related carrying value was reclassified to common stock and additional paid-in capital.

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 that utilizes a proprietary technology platform to discover and develop novel peptide-based drugs to address significant unmet medical needs and transform existing treatment paradigms for patients. We have three assets in various stages of clinical development derived from this platform, and we expect to report results from six different Phase 2 studies by the end of 2021.

Our most advanced clinical asset, PTG-300, is an injectable hepcidin mimetic in development for the potential treatment of iron overload and other blood disorders. PTG-300 mimics the effect of the natural hormone hepcidin, but with greater potency, solubility and stability. Hepcidin is a key hormone in regulating iron equilibrium and is critical to the proper development of red blood cells. We are currently developing PTG-300 for the treatment of ineffective erythropoiesis, chronic anemia and iron overload, with an initial focus on beta-thalassemia non-transfusion dependent ("NTD") and transfusion dependent ("TD") patients where the primary endpoints are hemoglobin increases and transfusion burden reductions, respectively. PTG-300 has received an orphan drug designation from the U.S. Food and Drug Administration ("FDA") and European Union ("EU") regulatory authorities for the treatment of beta-thalassemia. The FDA has granted Fast Track designation to PTG-300 for the treatment of beta-thalassemia. In the first quarter of 2019, we began dosing patients in a global Phase 2 study of PTG-300 in beta-thalassemia. Preliminary results from this Phase 2 study reported in the fourth quarter of 2019 suggest that the dose related pharmacodynamic responses in lowering serum iron and transferrin saturation ("TSAT") warrant continued evaluation at higher and/or more frequent doses which will be required to evaluate the rate and durability of clinical response in order to reach definitive conclusions. We expect to report clinical efficacy results from this Phase 2 study in 2020. We initiated a Phase 2 study in polycythemia vera ("PV") in the third quarter of 2019 and a Phase 2 study in hereditary hemochromatosis ("HH") in January 2020. We are working toward the initiation of an investigator-sponsored study ("IST") of PTG-300 in patients with myelodysplastic syndromes ("MDS") in the first half of 2020. Assuming PTG-300 shows clinical efficacy in one or more of the above indications, we intend to select our first indication in 2020 for a potential pivotal study to begin in 2021.

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

PTG-200 (also referenced as JNJ-67864238) is an orally delivered gut-restricted Interleukin-23 receptor ("IL-23R") antagonist for the treatment of IBD. In May 2017, we entered into a worldwide license and collaboration agreement with Janssen Biotech, Inc. ("Janssen"), a Johnson & Johnson company, to co-develop and co-detail PTG-200 and any second-generation compounds for all indications, including IBD. The agreement with Janssen was amended in May 2019 to expand the collaboration by supporting efforts towards second-generation IL-23R antagonists, triggering a $25.0 million milestone payment to us. In January 2020, as part of the expanded research collaboration, we announced the identification and nomination of an orally delivered, gut-restricted IL-23R antagonist peptide as a second-generation development candidate, triggering a $5.0 million milestone payment to us. See Note 3 to the Consolidated Financial Statements included elsewhere in this Annual Report on Form 10-K for additional information. In 2018, we completed a Phase 1 clinical study to evaluate the safety, pharmacokinetics and pharmacodynamics of PTG-200 in healthy

volunteers. Janssen submitted a U.S. Investigational New Drug application ("IND") for PTG-200 in CD during the second quarter of 2019, which took effect in July 2019. In collaboration with Janssen, we initiated a Phase 2 clinical study for PTG-200 in CD in the fourth quarter of 2019, with results expected in the first half of 2021.

PN-943 is an orally delivered, gut-restricted, alpha-4-beta-7 ("α4β7") specific integrin antagonist. We developed PN-943 as a potentially more potent orally delivered, gut-restricted α4β7 backup compound to PTG-100, our first-generation orally delivered gut-restricted α4β7 inhibitor that was being developed for treatment of UC. In 2019, we completed a Phase 1 single ascending dose ("SAD") and multiple ascending dose ("MAD") clinical study of PN-943 in healthy volunteers to evaluate safety, pharmacokinetics and pharmacodynamics. We reported results of the SAD part of the study during the second quarter of 2019 and the MAD part of the study during the third quarter of 2019. The pharmacodynamic results indicated that the administration of PN-943 was well tolerated, and results of target engagement were supportive of the higher potency of PN-943 as compared to PTG-100. We submitted a U.S. IND for PN-943 in December 2019, which took effect in January 2020. We anticipate initiating a Phase 2 proof of concept ("POC") study in UC in the second quarter of 2020, with topline data expected in the second half of 2021.

Our clinical assets are all derived from our proprietary discovery platform. Our platform enables us to engineer novel, structurally constrained peptides that retain key advantages of both orally delivered small molecules and injectable antibody drugs, while overcoming many of their limitations as therapeutic agents. Importantly, constrained peptides can be designed to alleviate the fundamental instability inherent in traditional peptides to allow different delivery forms, such as oral, subcutaneous, intravenous, and rectal. We continue to use our peptide technology platform to discover product candidates against targets in disease areas with significant unmet medical needs.

Operations

We have incurred net losses in each year since inception and we do not anticipate achieving sustained profitability in the foreseeable future. Our net losses were $77.2 million, $38.9 million and $37.0 million for the years ended December 31, 2019, 2018 and 2017, respectively. As of December 31, 2019, we had an accumulated deficit of $217.7 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 our worldwide license and collaboration agreement with Janssen, 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.

Janssen License and Collaboration Agreement

On May 26, 2017, we and Janssen, one of the Janssen Pharmaceutical Companies of Johnson & Johnson, entered into an exclusive license and collaboration agreement for the clinical development, manufacture and potential commercialization of PTG-200 worldwide for the treatment of CD and UC (the "Janssen License and Collaboration Agreement"), which was subsequently amended effective May 7, 2019 (the "First Amendment"). Janssen is a related party to us as Johnson & Johnson Innovation - JJDC, Inc., a significant stockholder of ours, and Janssen are both subsidiaries of Johnson & Johnson. During the third quarter of 2017, we received a non-refundable, upfront cash payment of $50.0 million from Janssen. During the second quarter of 2019, we received a non-refundable cash payment of $25.0 million upon execution of the First Amendment. During the fourth quarter of 2019, we became eligible to receive a cash payment of $5.0 million upon the successful nomination of a second-generation development candidate. See Note 3 to the Consolidated Financial Statements included elsewhere in this Annual Report on Form 10-K for additional information.

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.

Leases

We adopted Accounting Standards Codification Topic 842, *Leases,* ("ASC 842") effective January 1, 2019. We determine if an arrangement is a lease at inception. Pursuant to ASC 842, operating leases are included in operating lease right-of-use ("ROU") assets, operating lease liabilities, and noncurrent operating lease liabilities on the consolidated balance sheets. Operating lease ROU assets and operating lease liabilities are recognized based on the present value of the future minimum lease payments over the lease term at commencement date. If our leases do not provide an implicit rate, we use our incremental borrowing rate based on the information available at commencement date in determining the present value of future payments. The operating lease ROU asset also includes any lease payments made and excludes lease incentives and initial direct costs incurred. Lease terms include options to extend or terminate the lease when it is reasonably certain that we will exercise that option. Lease expense for minimum lease payments is recognized on a straight-line basis over the lease term.

We record tenant improvement allowances as a reduction to the ROU asset with the impact of the decrease recognized prospectively over the remaining lease term. The leasehold improvements will be amortized over the shorter of their useful life or the remaining term of the lease.

Revenue Recognition

We follow Accounting Standards Codification Topic 606, Revenue from Contracts with Customers ("ASC 606"). 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 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 we transfer to the customer. At contract inception, we assess the goods or services promised within each contract, 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 obligations when (or as) the performance obligations are satisfied. We constrain our estimate of the transaction price up to the amount (the "variable consideration constraint") that a significant reversal of recognized revenue is not probable.

Licenses of intellectual property: If a license to our intellectual property is determined to be distinct from the other performance obligations identified in an arrangement, we recognize revenue from non-refundable, upfront 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, upfront 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 or amendment 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. If there is more than one performance obligation, the transaction price is then allocated to each performance obligation on a relative stand-alone selling price basis. 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.

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).

Upfront 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. Amounts payable to us and not yet billed to the collaboration partner are recorded as contract assets. 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.

Contractual cost sharing payments made to a customer or collaboration partner are accounted for as a reduction to the transaction price if such payments are not related to distinct goods or services received from the customer or collaboration partner.

Contracts may be amended to account for changes in contract specifications and requirements. Contract modifications exist when the amendment either creates new, or changes existing, enforceable rights and obligations. When contract modifications create new performance obligations and the increase in consideration approximates the standalone selling price for goods and services related to such new performance obligations as adjusted for specific facts and circumstances of the contract, the modification is considered to be a separate contract and revenue is recognized prospectively. If a contract modification is not accounted for as a separate contract, we account for the promised goods or services not yet transferred at the date of the contract modification (the remaining promised goods or services) prospectively, as if it were a termination of the existing contract and the creation of a new contract, if the remaining goods or services are distinct from the goods or services transferred on or before the date of the contract modification. We account for a contract modification as if it were a part of the existing contract if the remaining goods or services are not distinct and, therefore, form part of a single performance obligation that is partially satisfied at the date of the contract modification. In such case the effect that the contract modification has on the transaction price, and on the entity's measure of progress toward complete satisfaction of the performance obligation, is recognized as an adjustment to revenue (either as an increase in or a reduction of revenue) at the date of the contract modification (the adjustment to revenue is made on a cumulative catch-up basis).

The period between when we transfer control of promised goods or services and when we receive payment is expected to be one year or less, and that expectation is consistent with our historical experience. Upfront payment contract liabilities resulting from our license and collaboration agreements do not represent a financing component as the payment is not financing the transfer of goods and services, and the technology underlying the licenses granted reflects research and development expenses already incurred by us. As such, we do not adjust our revenues for the effects of a significant financing component.

Stock-Based Compensation

We recognize compensation costs related to stock options accounted for under Accounting Standards Codification Topic 718 – "*Stock Compensation"* based on the estimated fair value of the awards on the date of grant. 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 subjective assumptions which determine the fair value of stock-based awards. Expected volatility generally requires significant judgement to determine. Our 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. We will continue to apply this process until a sufficient amount of historical information regarding the volatility of our own stock price becomes available.

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.

At December 31, 2019, our total gross deferred tax assets were $55.2 million and our gross deferred tax liabilities were $1.3 million. Due to our lack of earnings history and uncertainties surrounding our ability to generate future taxable income, our U.S. net deferred tax assets have been offset by a valuation allowance of $52.5 million. The deferred tax assets were primarily comprised of federal and state tax net operating loss and tax credit carryforwards. At December 31, 2019, we had $164.1 million of federal net operating loss carryforwards and $151.1 million of state net operating loss carryforwards. $78.7 million of the federal net operating loss carryforwards will begin to expire in 2033, if not utilized, and the remaining $85.4 million have not expiration date. The state net operating loss carryforwards will begin to expire in 2035, if not utilized. As of December 31, 2019, we also had accumulated Australian tax losses of AUD 13.1 million ($9.2 million) available for carry forward against future earnings, which under relevant tax laws do not expire but may not be available under certain circumstances.

Utilization of the net operating loss carryforwards may be subject to a substantial annual limitation due to ownership changes that may have occurred or that could occur in the future, as required by Section 382 of the Internal Revenue Code (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.

Recent Accounting Pronouncements

Information regarding recent accounting pronouncements applicable to us is included in Note 2 to the Consolidated Financial Statements included elsewhere in this Annual Report on Form 10-K.

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

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, information technology, 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 research and development tax incentives are recognized when there is reasonable assurance that the incentives will be received, the relevant expenditure has been incurred and the amount of the consideration can be reliably measured. We evaluate our eligibility under the tax incentive program as of each balance sheet date and make accruals and related adjustments based on the most current and relevant data available. We may alternatively be eligible for a taxable credit in the form of a non-cash tax incentive.

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 currently have three clinical assets in various stages of clinical development. 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. During 2018, we elected to halt further development of PTG-100 and concurrently elected to replace further development of PTG-100 with PN-943 based on an assessment of pre-clinical data from PN-943. We continued to experience expenses and credits related to winding down the development and trials for PTG-100 in 2019. We initiated a Phase 1 study of PN-943 during the fourth quarter of 2018. We have presented separately in the table below costs associated with the PN-943 program beginning in December 2018.

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

	Year Ended December 31,		
	2019	2018	2017
	(Dollars in thousands)		
Clinical and development expense — PTG-300	$ 30,325	$ 14,304	$ 4,246
Clinical and development expense — PN-943	20,924	523	—
Clinical and development expense — PTG-200	9,414	16,120	2,079
Clinical and development expense — PTG-100	288	20,443	25,825
Milestone payment obligation to former collaboration partner	—	500	250
Pre-clinical and drug discovery research expense	4,162	9,837	15,292
Grants and incentives reimbursement of expenses, net	(110)	(2,230)	(1,511)
Total research and development expenses	$ 65,003	$ 59,497	$ 46,181

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 intensive. 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 are 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 continue to incur expenses to support our continued operations as a public company, including expenses related to existing and future compliance with rules and regulations of the SEC and those of the national securities exchange on which our securities are traded, insurance expenses, investor relations, professional services and general overhead and administrative costs.

Interest Income

Interest income consists of interest earned on our cash, cash equivalents, and marketable securities.

Interest Expense

Interest expense consists of interest recognized on our long-term debt, which is comprised of contractual interest, amortization of origination fees and other issuance costs, and accretion of final payment fees.

Other Expense, Net

Other expense, net consists primarily of amounts related to foreign exchange gains and losses and related items.

Results of Operations

Comparison of the Year ended December 31, 2019 and 2018

	Year Ended December 31,		Dollar Change	% Change
	2019	2018		
	(Dollars in thousands)			
License and collaboration revenue - related party	$ 231	$ 30,925	$ (30,694)	(99)
Operating expenses:				
Research and development [1]	65,003	59,497	5,506	9
General and administrative [2]	15,749	13,697	2,052	15
Total operating expenses	80,752	73,194	7,558	10
Loss from operations	(80,521)	(42,269)	(38,252)	90
Interest income	2,813	2,566	247	10
Interest expense	(169)	—	(169)	100
Other expense, net	(1)	(20)	19	(95)
Loss before income tax benefit	(77,878)	(39,723)	(38,155)	96
Income tax benefit	691	799	(108)	(14)
Net loss	$ (77,187)	$ (38,924)	$ (38,263)	98

[1] Includes $4.4 million and $3.4 million of non-cash stock-based compensation expense for the year ended December 31, 2019 and 2018, respectively.

[2] Includes $4.0 million and $3.5 million of non-cash stock-based compensation expense for the year ended December 31, 2019 and 2018, respectively.

License and Collaboration Revenue

License and collaboration revenue decreased $30.7 million, or 99%, from $30.9 million for the year ended December 31, 2018 to $0.2 million for the year ended December 31, 2019. The decrease in license and collaboration revenue was primarily due to a contract modification for the First Amendment to the Janssen License and Collaboration Agreement and the related cumulative catchup adjustment during the second quarter of 2019. The contract modification resulted in an increase in the transaction price and additional deliverables under the performance obligation, leading to an overall corresponding decrease in the cumulative percentage of completion of our performance obligation for the Janssen License and Collaboration Agreement.

We determined that the transaction price of the Janssen License and Collaboration Agreement was $112.9 million as of December 31, 2019, an increase of $52.2 million from the transaction price of $60.7 million at December 31, 2018. In order to determine the transaction price, we evaluated all payments to be received during the duration of the contract, net of Phase 2 development costs reimbursement expected to be payable to Janssen. We determined that the transaction price includes the $50.0 million upfront payment, the $25.0 million payment received upon the effectiveness of the First Amendment, the $5.0 million payment triggered by the successful nomination of a second-generation compound, $18.3 million of reimbursement from Janssen for services performed for PTG-200 Phase 2 and for second-generation compound research costs and other services, and $14.6 million of estimated variable consideration, which includes a $7.5 million milestone payment subject to the completion of a Phase 1 study for a second-generation compound. The increase in transaction price from December 31, 2018 to December 31, 2019 was due to an increase in fixed and variable consideration related to the contract modification for First Amendment to the Janssen License and Collaboration Agreement effective May 7, 2019. We re-evaluate the transaction price each reporting period and as uncertain events are resolved or other changes in circumstances occur.

Research and Development Expenses

Research and development expenses increased $5.5 million, or 9%, from $59.5 million for the year ended December 31, 2018 to $65.0 million for the year ended December 31, 2019. The increase included $20.4 million of PN-943 clinical trial and development expenses, an increase of $16.0 million in PTG-300 clinical trial and development expenses and a $1.3 million reversal of previously recorded reductions to research and development expenses in connection with the tax incentive from Australia, partially offset by a decrease of $20.1 million in PTG-100 clinical trial and development expenses due to the halting of further development during 2018 and related credit adjustments, a decrease of $6.7 million for PTG-200 clinical trial and development expenses under the Janssen License and Collaboration Agreement due to timing of deliverables and a decrease of $5.7 million in pre-clinical and discovery research expenses. Research and development expenses for the year ended December 31, 2019 included increased personnel costs due to an increase in research and development headcount from 49 employees at December 31, 2018 to 54 employees at December 31, 2019.

General and Administrative Expenses

General and administrative expenses increased $2.0 million, or 15%, from $13.7 million for the year ended December 31, 2018 to $15.7 million for the year ended December 31, 2019 primarily due to increases of $1.0 million in personnel costs to support the growth of our operations, $0.7 million in professional fees and $0.3 million in insurance expense. The increase in personnel costs for the year ended December 31, 2019 reflected an increase in general and administrative headcount from 15 employees at December 31, 2018 to 19 employees at December 31, 2019.

Interest Income

Interest income increased $0.2 million, or 10%, from $2.6 million for the year ended December 31, 2018 to $2.8 million for the year ended December 31, 2019 primarily due to higher interest income related to an increase in marketable securities balances.

Income Tax Benefit

Income tax benefit decreased $0.1 million, or 14%, from $0.8 million for the year ended December 31, 2018, representing an effective income tax rate of 2.0%, to $0.7 million for the year ended December 31, 2019, representing an effective income tax rate of 0.9%. Our effective income tax rate differs from our federal statutory rate of 21%, primarily because our U.S. loss cannot be benefited due to the full valuation allowance position and reduced by foreign taxes.

Comparison of the Years ended December 31, 2018 and 2017

	Year Ended December 31,		Dollar Change	% Change
	2018	2017		
	(Dollars in thousands)			
License and collaboration revenue - related party	$ 30,925	$ 20,063	$ 10,862	54
Operating expenses:				
Research and development [1]	59,497	46,181	13,316	29
General and administrative [2]	13,697	11,779	1,918	16
Total operating expenses	73,194	57,960	15,234	26
Loss from operations	(42,269)	(37,897)	(4,372)	12
Interest income	2,566	948	1,618	171
Other expense, net	(20)	(8)	(12)	150
Loss before income tax benefit	(39,723)	(36,957)	(2,766)	7
Income tax benefit	799	—	799	100
Net loss	$ (38,924)	$ (36,957)	$ (1,967)	5

(1) Includes $3.4 million and $2.0 million of non-cash stock-based compensation expense for the year ended December 31, 2018 and 2017, respectively.
(2) Includes $3.5 million and $2.2 million of non-cash stock-based compensation expense for the year ended December 31, 2018 and 2017, respectively.

License and Collaboration Revenue

License and collaboration revenue increased $10.8 million, or 54%, from $20.1 million for the year ended December 31, 2017 to $30.9 million for the year ended December 31, 2018. The increase was primarily due to deferred revenue and cost sharing revenue recognized in connection with the completion of Phase 1 activities and delivery of compound supply services for Phase 2a activities under the Janssen License and Collaboration Agreement, which became effective in July 2017.

We determined that the transaction price of the Janssen License and Collaboration Agreement was $60.7 million as of December 31, 2018, an increase of $6.8 million from the transaction price of $53.9 million at December 31, 2017. In order to determine the transaction price, we evaluated all 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 IND, which was fully constrained as of December 31, 2018, and $10.7 million of estimated variable consideration for cost-sharing payments from Janssen for agreed upon services related to Phase 2a activities as of December 31, 2018 constituted consideration to be included in the transaction price, which is to be allocated to the combined performance obligation. The increase in transaction price was due to an increase in variable consideration related to compound supply services, which was recognized as a cumulative catch-up adjustment. During the year ended December 31, 2018, this increased overall variable consideration by $6.8 million and extended our projected completion date into the first half of 2019. We will re-evaluate the transaction price at each reporting period and as uncertain events are resolved or other changes in circumstances occur.

Research and Development Expenses

Research and development expenses increased $13.3 million, or 29%, from $46.2 million for the year ended December 31, 2017 to $59.5 million for the year ended December 31, 2018. The increase was primarily due to $14.0 million for PTG-200 Phase 1 clinical trial and development expenses, $10.1 million for PTG-300 Phase 1 clinical trial and development expenses, $0.5 million for PN-943 Phase 1 clinical trial and development expenses and an increase of $0.3 million in milestone payments to a former collaboration partner. These increases were partially offset by a decrease of $5.5 million in pre-clinical and discovery research expense, including pre-clinical development activities for PTG-200, PTG-300 PN-943 and our other product candidates, a decrease of $5.4 million in PTG-100 Phase 1 clinical trial and development expenses and a decrease of $0.7 million in expense reimbursement under grants and incentives. Research and development expenses for the year ended December 31, 2018 include an increase in personnel costs due to increased research and development headcount from 44 employees at December 31, 2017 to 49 employees at December 31, 2018.

General and Administrative Expenses

General and administrative expenses increased $1.9 million, or 16%, from $11.8 million for the year ended December 31, 2017, to $13.7 million for the year ended December 31, 2018. The increase was primarily due to an increase of $2.4 million in personnel costs to support the growth of our operations, partially offset by a $0.5 million decrease in legal fees primarily related to the Janssen License and Collaboration Agreement. The increase in personnel costs for the year ended December 31, 2018 reflected an increase in general and administrative headcount from 11 employees at December 31, 2017 to 15 employees at December 31, 2018 and included a $1.3 million increase in stock-based compensation expense.

Interest Income

Interest income increased $1.6 million, or 171%, from $0.9 million for the year ended December 31, 2017 to $2.5 million for the year ended December 31, 2018. The increase in interest income was primarily due to the increasing interest rate environment during the year ended December 31, 2018.

Income Tax Benefit

Income tax benefit for the year ended December 31, 2018 was $0.8 million. The income tax benefit was due primarily to the 2018 release of the valuation allowance related to Protagonist Australia. We believe these deferred tax assets will be realized in the future due to expected profitability for this subsidiary. No income tax provision was recorded for the year ended December 31, 2017.

Liquidity and Capital Resources

Liquidity and Capital Expenditures

As of December 31, 2019, we had $133.0 million of cash, cash equivalents and marketable securities and an accumulated deficit of $217.7 million. Our operations have been financed by net proceeds from the sale of shares of our capital stock, payments under the Janssen License and Collaboration Agreement and proceeds from our long-term debt. During the third quarter of 2017 we received a non-refundable, upfront payment of $50.0 million from Janssen. During the second quarter of 2019, we received a nonrefundable $25.0 million payment from Janssen upon execution of the First Amendment. During the fourth quarter of 2019, we became eligible to receive a nonrefundable $5.0 million payment from Janssen, which we received during the first quarter of 2020.

In September 2017, we filed a registration statement on Form S-3 with the Securities and Exchange Commission (File No. 333-220314) that was declared effective as of October 5, 2017 and permits the offering, issuance, and sale by us of up to a maximum aggregate offering price of $200.0 million of our common stock, preferred stock and certain debt securities (the "2017 Form S-3"). 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 ("ATM") financing facility under a sales agreement (the "2017 Sales Agreement"). The 2017 Sales Agreement was terminated in 2019. During the year ended December 31, 2019, prior to the termination of the 2017 Sales Agreement, we sold 2,846,641 shares of our common stock for net proceeds of $34.5 million, after deducting issuance costs. We sold 151,273 shares of our common stock pursuant to the 2017 Sales Agreement during the year ended December 31, 2018 for net proceeds of $1.5 million, after deducting issuance costs. As of December 31, 2019, $72.0 million of common stock remained available for sale under the 2017 Form S-3.

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 paid by us, were $64.5 million.

In August 2018, we entered into a Securities Purchase Agreement with certain accredited investors (each, an "Investor" and, collectively, the "Investors"), pursuant to which we sold an aggregate of 2,750,000 shares of our common stock at a price of $8.00 per share, for aggregate net proceeds of $21.7 million, after deducting offering expenses payable by us. In a concurrent private placement, we issued the Investors warrants to purchase an aggregate of 2,750,000 shares of our common stock (each, a "Warrant" and, collectively, the "Warrants"). Each Warrant is exercisable from August 8, 2018 through August 8, 2023. Warrants to purchase 1,375,000 shares of our common stock have an exercise price of $10.00 per share and Warrants to purchase 1,375,000 shares of our common stock have an exercise price of $15.00 per share. The exercise price and number of shares of common stock issuable upon the exercise of the Warrants (the "Warrant Shares") are subject to adjustment in the event of any stock dividends and splits, reverse stock split, recapitalization, reorganization or similar transaction, as described in the Warrants. Under certain circumstances, the Warrants may be exercisable on a "cashless" basis. In connection with the issuance and sale of the common stock and Warrants, we granted the Investors certain registration rights with respect to the Warrants and the

Warrant Shares. The common stock and Warrants are classified as equity in accordance with Accounting Standards Codification Topic 480*, Distinguishing Liabilities from Equity* ("ASC 480"), and the net proceeds from the transaction were recorded as a credit to additional paid-in capital. As of December 31, 2019, none of the Warrants have been exercised.

In December 2018, we entered into an exchange agreement (the "Exchange Agreement") with an Investor and its affiliates (the "Exchanging Stockholders"), pursuant to which we exchanged an aggregate of 1,000,000 shares of our common stock, par value $0.00001 per share, owned by the Exchanging Stockholders for pre-funded warrants (the "Exchange Warrants") to purchase an aggregate of 1,000,000 shares of common stock (subject to adjustment in the event of any stock dividends and splits, reverse stock split, recapitalization, reorganization or similar transaction, as described in the Exchange Warrants), with an exercise price of $0.00001 per share. The Exchange Warrants will expire ten years from the date of issuance. The Exchange Warrants are exercisable at any time prior to expiration except that the Exchange Warrants cannot be exercised by the Exchanging Stockholders if, after giving effect thereto, the Exchanging Stockholders would beneficially own more than 9.99% of our common stock, subject to certain exceptions. In accordance with Accounting Standards Codification Topic 505, *Equity* , we recorded the retirement of the common stock exchanged as a reduction of common stock shares outstanding and a corresponding debit to additional paid-in-capital at the fair value of the Exchange Warrants on the issuance date. The Exchange Warrants are classified as equity in accordance with ASC 480, and fair value of the Exchange Warrants was recorded as a credit to additional paid-in capital and is not subject to remeasurement. We determined that the fair value of the Exchange Warrants is substantially similar to the fair value of the retired shares on the issuance date due to the negligible exercise price for the Exchange Warrants. During the year ended December 31, 2019, Exchange Warrants to purchase 600,000 shares were net exercised, resulting in the issuance of 599,997 shares of common stock. As of December 31, 2019, 400,000 of the Exchange Warrants remain unexercised.

In October 2019, we filed a registration statement on Form S-3 (File no. 333-234414) that was declared effective as of November 22, 2019 and permits the offering, issuance, and sale by us of up to a maximum aggregate offering price of $250.0 million of our common stock, preferred stock, debt securities and warrants (the "2019 Form S-3"). Up to a maximum of $75.0 million of the maximum aggregate offering price of $250.0 million may be issued and sold pursuant to an ATM financing facility under a sales agreement we entered into on November 27, 2019 (the "2019 Sales Agreement"). As of December 31, 2019, no offering, issuance or sale of common stock, preferred stock, debt securities or warrants was made under the 2019 Form S-3 or the 2019 Sales Agreement.

In October 2019, we entered into a credit and security agreement pursuant to which the lenders party thereto agreed to make term loans available to us for working capital and general business purposes, in a principal amount of up to $50.0 million, including a $10.0 million term loan which was funded at closing (October 30, 2019), with the ability to access the remaining $40.0 million in two additional tranches of $20.0 million, subject to specified availability periods, the achievement of certain clinical development milestones, minimum cash requirements and other customary conditions. Additional information about this credit facility and our long-term debt is presented in Note 8 to the consolidated financial statements included elsewhere in this Annual Report on Form 10-K.

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 marketable securities and access to our debt facility 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 as well as seek additional collaborative or other arrangements with corporate sources 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 current 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, including any second-generation compounds, upon regulatory approval or clearance, if any;
- the amount and timing of sales and other revenues from our current 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;
- the costs of maintaining, expanding and protecting our intellectual property portfolio; and
- the costs of ongoing general and administrative activities to support the growth of our business.

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. 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,		
	2019	2018	2017
		(In thousands)	
Cash (used in) provided by operating activities	$ (41,527)	$ (49,947)	$ 3,872
Cash (used in) provided by investing activities	(53,710)	2,213	15,823
Cash provided by financing activities	46,036	24,115	65,554

Cash Flows from Operating Activities

Cash used in operating activities for the year ended December 31, 2019 was $41.5 million, consisting of our net loss of $77.2 million, partially offset by a net change of $26.1 million in net operating assets and liabilities and non-cash charges of $9.5 million. The change in net operating assets and liabilities was primarily due to a net increase of $33.5 million in deferred revenue related to the Janssen License and Collaboration Agreement, a decrease of $1.4 million in research and development tax incentive receivable and an increase of $1.1 million in accrued expenses and other payables, partially offset by an decrease of $3.0 million in accounts payable, an increase of $2.8 million in prepaid expenses and other assets, an increase of $2.2 million in receivable from collaboration partner and a decrease of $1.9 million in operating lease liability. Non-cash charges were primarily comprised of $8.4 million of stock-based compensation, $1.8 million of operating lease right-of-use asset amortization and $0.7 million of depreciation and amortization, partially offset by a $0.8 million increase in deferred tax assets and $0.6 million of net accretion of discount on marketable securities.

Cash used in operating activities for the year ended December 31, 2018 was $49.9 million, consisting of our net loss of $38.9 million and a net change of $18.0 million in net operating assets and liabilities, partially offset by non-cash charges of $7.0 million. The change in net operating assets and liabilities was primarily due to a net decrease of $23.5 million in deferred revenue related to the Janssen License and Collaboration Agreement and an increase of $2.8 million in receivable from collaboration partner, partially offset by an increase of $4.4 million in accounts payable, an increase of $1.9 million in accrued expenses and other payables, an increase of $1.1 million in payable to collaboration partner and a decrease of $1.1 million in prepaid expenses and other assets. Non-cash charges were primarily comprised of $6.9 million of stock-based compensation, $0.5 million of depreciation and amortization and $0.2 million of net amortization of premium on marketable securities, partially offset by a $0.7 million increase in deferred tax assets.

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 marketable securities and $0.4 million of depreciation and amortization.

Cash Flows from Investing Activities

Cash used in investing activities for the year ended December 31, 2019 was $53.7 million, consisting of purchases of marketable securities of $166.9 million and purchases of property and equipment of $1.0 million, partially offset by proceeds from maturities of marketable securities of $114.2 million. Purchases of property and equipment were primarily related to purchases of scientific equipment and leasehold improvements.

Cash provided by investing activities for the year ended December 31, 2018 was $2.2 million, consisting of proceeds from marketable securities of $73.8 million, partially offset by purchases of marketable securities of $71.1 million and purchases of property and equipment of $0.5 million. Purchases of property and equipment were primarily related to purchases of scientific equipment.

Cash provided by investing activities for the year ended December 31, 2017 was $15.8 million, consisting of proceeds from maturities of marketable securities of $56.0 million, partially offset by purchases of marketable 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 Flows from Financing Activities

Cash provided by financing activities for the year ended December 31, 2019 was $46.0 million, consisting of $34.5 million of net proceeds from sales of common stock through our ATM financing facility, $9.8 million of net proceeds from long-term debt and $1.8 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, 2018 was $24.1 million, consisting of $21.7 million of net proceeds from issuance of our common stock and warrants in a private placement, $1.5 million of net proceeds from sales through our ATM financing facility and $0.9 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, 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.

Contractual Obligations and Other Commitments

The following table summarizes our future minimum contractual obligations as of December 31, 2019.

	Payments Due by Period				
Contractual Obligations:	**Less Than 1 Year**	**1 to 3 Years**	**3 to 5 Years**	**More Than 5 Years**	**Total**
			(In thousands)		
Debt payment obligations [1]	$ —	$ 5,833	$ 4,452	$ —	$ 10,285
Operating lease obligations [2]	1,941	4,059	3,016	—	9,016
Total contractual obligations	$ 1,941	$ 9,892	$ 7,468	$ —	$ 19,301

[1] Represents principal and final payment fee on our long-term debt. See Note 8 to the consolidated financial statements included elsewhere in this Annual Report on Form 10-K for additional information.

[2] Represents minimum lease payments under our operating lease obligations. See Note 9 to the consolidated financial statements elsewhere in this Annual Report on Form 10-K for additional information.

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. We did not record any research and development expense under this agreement for the year ended December 31, 2019. For the years ended December 31, 2018 and 2017, we recorded research and development expense of $500,000 and $250,000, respectively, under this agreement. 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, Zealand could be eligible to receive up to an additional aggregate of $128.0 million for the achievement of certain development, regulatory and sales milestone events. In addition, Zealand could be eligible to receive 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 related to our investments and borrowings.

We had $133.0 million and $128.9 million in cash, cash equivalents and marketable securities at December 31, 2019 and December 31, 2018, respectively. Cash and cash equivalents consist of cash, money market funds, commercial paper and government bonds. Marketable securities consist of corporate bonds, commercial paper and government bonds. A portion of our investments may be subject to interest rate risk and could fall in value if market interest rates increase. We had $9.8 million in long-term debt at December 31, 2019, which bears interest at an annual rate of prime plus 2.91%, with a 4.94% prime rate floor. Based on our interest rate sensitivity analysis, a 1% increase or decrease in interest rates would have a net impact of approximately $1.0 million on our results of operations.

Approximately $0.6 million and $0.4 million of our cash balance was located in Australia at December 31, 2019 and December 31, 2018, 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 (the "Company") as of December 31, 2019 and 2018, and the related consolidated statements of operations, comprehensive loss, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2019, 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, 2019 and 2018, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2019 in conformity with accounting principles generally accepted in the United States of America.

Change in Accounting Principle

As discussed in Note 2 to the consolidated financial statements, the Company changed the manner in which it accounts for leases in 2019.

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 10, 2020

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

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

	December 31, 2019	December 31, 2018
Assets		
Current assets:		
Cash and cash equivalents	$ 33,006	$ 82,233
Marketable securities	100,011	46,620
Restricted cash - current	10	10
Receivable from collaboration partner and contract asset - related party	6,755	4,587
Research and development tax incentive receivable, net	—	1,429
Prepaid expenses and other current assets	5,529	2,624
Total current assets	145,311	137,503
Property and equipment, net	1,681	861
Restricted cash - noncurrent	450	450
Operating lease right-of-use asset	6,042	—
Deferred tax asset	1,433	658
Total assets	$ 154,917	$ 139,472
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 2,790	$ 5,711
Payable to collaboration partner - related party	1,262	1,061
Accrued expenses and other payables	12,360	11,163
Deferred revenue - related party - current	17,738	8,223
Operating lease liability - current	1,256	—
Total current liabilities	35,406	26,158
Long-term debt, net	9,794	—
Deferred revenue - related party - noncurrent	23,792	—
Operating lease liability - noncurrent	5,961	—
Deferred rent	—	799
Total liabilities	74,953	26,957
Commitments and contingencies (Note 10)		
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; 27,217,649 and 23,187,219 shares issued and outstanding as of December 31, 2019 and December 31, 2018, respectively	—	—
Additional paid-in capital	297,846	253,222
Accumulated other comprehensive loss	(221)	(233)
Accumulated deficit	(217,661)	(140,474)
Total stockholders' equity	79,964	112,515
Total liabilities and stockholders' equity	$ 154,917	$ 139,472

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,		
	2019	2018	2017
License and collaboration revenue - related party	$ 231	$ 30,925	$ 20,063
Operating expenses:			
Research and development	65,003	59,497	46,181
General and administrative	15,749	13,697	11,779
Total operating expenses	80,752	73,194	57,960
Loss from operations	(80,521)	(42,269)	(37,897)
Interest income	2,813	2,566	948
Interest expense	(169)	—	—
Other expense, net	(1)	(20)	(8)
Loss before income tax benefit	(77,878)	(39,723)	(36,957)
Income tax benefit	691	799	—
Net loss	$ (77,187)	$ (38,924)	$ (36,957)
Net loss per share, basic and diluted	$ (2.98)	$ (1.74)	$ (2.09)
Weighted-average shares used to compute net loss per share, basic and diluted	25,894,024	22,364,515	17,694,505

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,		
	2019	2018	2017
Net loss	$ (77,187)	$ (38,924)	$ (36,957)
Other comprehensive loss:			
(Loss) gain on translation of foreign operations	(44)	(322)	298
Unrealized gain (loss) on marketable securities	56	95	(59)
Comprehensive loss	$ (77,175)	$ (39,151)	$ (36,718)

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

PROTAGONIST THERAPEUTICS, INC.
Consolidated Statements of Stockholders' Equity
(In thousands, except share and per share data)

	Common Stock		Additional Paid-In Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
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
Issuance of common stock upon under equity incentive and employee stock purchase plans	306,526	—	1,007	—	—	1,007
Stock-based compensation expense	—	—	4,241	—	—	4,241
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
Issuance of common stock and warrants upon private placement, net of issuance costs	2,750,000	—	21,673	—	—	21,673
Issuance of common stock under equity incentive and employee stock purchase plans	197,640	—	934	—	—	934
Issuance of common stock pursuant to at-the-market offering, net of issuance costs	151,273	—	1,508	—	—	1,508
Retirement of common stock in exchange for common stock warrant.	(1,000,000)	—	(6,670)	—	—	(6,670)
Issuance of common stock warrant in exchange for retirement of common stock	—	—	6,670	—	—	6,670
Stock-based compensation expense	—	—	6,919	—	—	6,919
Other comprehensive loss	—	—	—	(227)	—	(227)
Net loss	—	—	—	—	(38,924)	(38,924)
Balance at December 31, 2018	23,187,219	—	253,222	(233)	(140,474)	112,515
Issuance of common stock pursuant to at-the-market offering, net of issuance costs	2,846,641	—	34,492	—	—	34,492
Issuance of common stock under equity incentive and employee stock purchase plans	583,792	—	1,779	—	—	1,779
Issuance of common stock upon exercise of Exchange Warrants	599,997	—	—	—	—	—
Stock-based compensation expense	—	—	8,353	—	—	8,353
Other comprehensive gain	—	—	—	12	—	12
Net loss	—	—	—	—	(77,187)	(77,187)
Balance at December 31, 2019	27,217,649	$ —	$ 297,846	$ (221)	$ (217,661)	$ 79,964

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,		
	2019	2018	2017
CASH FLOWS FROM OPERATING ACTIVITIES			
Net loss	$ (77,187)	$ (38,924)	$ (36,957)
Adjustments to reconcile net loss to net cash (used in) provided by operating activities:			
Stock-based compensation	8,353	6,919	4,241
Operating lease right-of-use asset amortization	1,792	—	—
Depreciation and amortization	703	527	406
Amortization of issuance costs and accretion of final payment fee for long-term debt	29	—	—
Gain (loss) on disposal of property and equipment	8	—	(62)
Net (accretion of discount) amortization of premium on marketable securities	(594)	206	687
Change in deferred tax asset	(775)	(658)	—
Changes in operating assets and liabilities:			
Research and development tax incentive receivable, net	1,411	(236)	1,070
Receivable from collaboration partner - related party	(2,168)	(2,771)	(1,816)
Prepaid expenses and other assets	(2,820)	1,117	(333)
Accounts payable	(3,000)	4,430	91
Payable to collaboration partner - related party	201	1,061	—
Accrued expenses and other payables	1,098	1,911	4,793
Deferred revenue - related party	33,307	(23,529)	31,752
Operating lease liability	(1,885)	—	—
Net cash (used in) provided by operating activities	(41,527)	(49,947)	3,872
CASH FLOWS FROM INVESTING ACTIVITIES			
Purchase of marketable securities	(166,936)	(71,060)	(39,546)
Proceeds from maturities of marketable securities	114,193	73,759	56,035
Purchases of property and equipment, net	(967)	(486)	(666)
Net cash (used in) provided by investing activities	(53,710)	2,213	15,823
CASH FLOWS FROM FINANCING ACTIVITIES			
Proceeds from at-the-market offering, net of issuance costs	34,492	1,508	—
Proceeds from issuance of long-term debt, net of issuance costs	9,765	—	—
Proceeds from issuance of common stock upon exercise of stock options and purchases under employee stock purchase plan	1,779	934	1,007
Proceeds from issuance of common stock and warrants in private placement, net of issuance costs	—	21,673	64,547
Net cash provided by financing activities	46,036	24,115	65,554
Effect of exchange rate changes on cash, cash equivalents and restricted cash	(26)	(177)	146
Net (decrease) increase in cash, cash equivalents and restricted cash	(49,227)	(23,796)	85,395
Cash, cash equivalents and restricted cash, beginning of period	82,693	106,489	21,094
Cash, cash equivalents and restricted cash, end of period	$ 33,466	$ 82,693	$ 106,489
SUPPLEMENTAL DISCLOSURES OF CASH FLOW INFORMATION:			
Cash paid for interest	$ 70	$ —	$ —
SUPPLEMENTAL DISCLOSURES OF NON-CASH FINANCING AND INVESTING INFORMATION:			
Purchases of property and equipment in accounts payable and accrued liabilities	$ 100	$ 24	$ —
Deferred offering costs in accounts payable and accrued liabilities	$ 80	$ —	$ 66
Fair value of common stock retired in exchange for issuance of common stock warrant	$ —	$ 6,670	$ —
Acquisition of new equipment upon trade-in for existing equipment	$ —	$ —	$ 185

The accompanying notes are an integral part of these 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 that utilizes a proprietary technology platform to discover and develop novel peptide-based drugs to transform existing treatment paradigms for patients with 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 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 $217.7 million as of December 31, 2019. The Company's ultimate success depends on the outcome of its research and development and collaboration activities. The Company expects to incur additional losses in the future and anticipates the need to raise additional capital to continue to execute its long-range business plan. Since the Company's initial public offering in August 2016, it has financed its operations through offerings of common stock, payments received under a license and collaboration agreement and proceeds received from long-term debt.

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 Australia, 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 upon consolidation.

Certain prior period amounts have been reclassified to conform to the current year presentation. There was no effect on net loss or stockholders' equity related to these reclassifications.

The financial statements of Protagonist Australia 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, 2019 and 2018 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, stock-based compensation, income taxes, research and development tax incentives, marketable securities and leases. Estimates related to revenue recognition include actual costs incurred versus total estimated costs of the Company's deliverables to determine percentage of completion in addition to the application and estimates of potential revenue constraints in the determination of the transaction price under its license and collaboration agreements. 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 marketable securities. Substantially all of the Company's cash is held by two 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 marketable 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 marketable securities in fixed income securities denominated and payable in U.S. dollars. Permissible investments of fixed income securities include obligations of the U.S. 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.

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 a letter of credit related to the Company's facility lease entered into in March 2017 and the Company's corporate credit card.

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,		
	2019	2018	2017
Cash and cash equivalents	$ 33,006	$ 82,233	$ 106,029
Restricted cash - current	10	10	10
Restricted cash - noncurrent	450	450	450
Cash balance in consolidated statements of cash flows	$ 33,466	$ 82,693	$ 106,489

Marketable 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 greater than three months but not longer than 365 days as of the balance sheet date. Long-term marketable securities have maturities of 365 days or longer 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, payable to collaboration partner and accrued expenses and other payables approximate fair value due to their short-term maturities. See Note 4. to the Consolidated Financial Statements for additional information 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.

Leases

The Company adopted Accounting Standards Codification Topic 842, *Leases,* ("ASC 842") effective January 1, 2019. The Company determines if an arrangement is a lease at inception. Pursuant to ASC 842, operating leases are included in operating lease right-of-use ("ROU") assets, operating lease liabilities, and noncurrent operating lease liabilities on the consolidated balance sheets. Operating lease ROU assets and operating lease liabilities are recognized based on the present value of the future minimum lease payments over the lease term at commencement date. If the Company's leases do not provide an implicit rate, the Company uses its incremental borrowing rate based on the information available at commencement date in determining the present value of future payments. The operating lease ROU asset also includes any lease payments made and excludes lease incentives and initial direct costs incurred. Lease terms include options to extend or terminate the lease when it is reasonably certain that the Company will exercise that option. Lease expense for minimum lease payments is recognized on a straight-line basis over the lease term.

The Company records tenant improvement allowances as a reduction to the ROU asset with the impact of the decrease recognized prospectively over the remaining lease term. The leasehold improvements will be amortized over the shorter of their useful life or the remaining term of the lease.

Impairment of Long-Lived Assets

The Company reviews long-lived assets, primarily comprised of property, equipment and operating lease right-of-use assets, 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.

Long Term Debt

The Company accounts for interest on its long-term debt under the effective interest method, with interest expense comprised of contractual interest, amortization of origination fees and other issuance costs, and accretion of final payment fees.

Comprehensive Loss

Comprehensive loss includes net loss as well as other changes in stockholders' equity 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 a 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

The Company follows Accounting Standards Codification Topic 606, *Revenue from Contracts with Customers* ("ASC 606"). 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 applies the five-step model to contracts when it is probable that the Company will collect the

consideration it is entitled to in exchange for the goods or services it transfers to the customer. At contract inception, the Company assesses the goods or services promised within each contract, 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 obligations when (or as) the performance obligations are satisfied. The Company constrains its estimate of the transaction price up to the amount (the "variable consideration constraint") that a significant reversal of recognized revenue is not probable.

Licenses of intellectual property: If a license to the Company's intellectual property is determined to be distinct from the other performance obligations identified in an arrangement, the Company recognizes revenue from non-refundable, upfront 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 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, upfront 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 or amendment 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. If there is more than one performance obligation, 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.

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).

Upfront 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. Amounts payable to the Company and not yet billed to the collaboration partner are recorded as contract assets. 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.

Contractual cost sharing payments made to a customer or collaboration partner are accounted for as a reduction to the transaction price if such payments are not related to distinct goods or services received from the customer or collaboration partner.

Contracts may be amended to account for changes in contract specifications and requirements. Contract modifications exist when the amendment either creates new, or changes existing, enforceable rights and obligations. When contract modifications create new performance obligations and the increase in consideration approximates the standalone selling price for goods and services related to such new performance obligations as adjusted for specific facts and circumstances of the contract, the modification is considered to be a separate contract. If a contract modification is not accounted for as a separate contract, the Company accounts for the promised goods or services not yet transferred at the date of the contract modification (the remaining promised goods or services) prospectively, as if it were a termination of the existing contract and the creation of a new contract, if the remaining goods or services are distinct from the goods or services transferred on or before the date of the contract modification. The Company accounts for a contract modification as if it were a part of the existing contract if the remaining goods or services are not distinct and, therefore, form part of a single performance obligation that is partially satisfied at the date of the contract modification. In such case the effect that the contract modification has on the transaction price, and on the entity's measure of progress toward complete satisfaction of the performance obligation, is recognized as an adjustment to revenue (either as an increase in or a reduction of revenue) at the date of the contract modification (the adjustment to revenue is made on a cumulative catch-up basis).

The period between when the Company transfers control of promised goods or services and when the Company receives payment is expected to be one year or less, and that expectation is consistent with the Company's historical experience. Upfront payment contract liabilities resulting from the Company's license and collaboration agreements do not represent a financing component as the payment is not financing the transfer of goods and services, and the technology underlying the licenses granted reflects research and development expenses already incurred by the Company. As such, the Company does not adjust its revenues for the effects of a significant financing component.

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 or otherwise. 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 pre-clinical 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. 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. 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, the rate of patient enrollment and number and location of sites activated 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 either a refundable cash tax incentive or a taxable credit in the form of a non-cash tax incentive from the Australian Taxation Office ("ATO"). The refundable cash 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 refundable cash 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. The Company may alternatively be eligible for a taxable credit in the form of a non-

cash tax incentive in years when the annual turnover exceeds the limit. The Company evaluates its eligibility under tax incentive programs as of each balance sheet date and makes accrual and related adjustments based on the most current and relevant data available.

SBIR Grants

The Company has received Small Business Innovation Research ("SBIR") grants from the National Institutes of Health ("NIH") in support of its research activities. The Company recognizes a reduction to research and development expenses when expenses related to grants have been incurred and the grant funds become contractually due from NIH.

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. For stock option awards, the Company uses the Black-Scholes option-pricing model to estimate fair values. For restricted stock unit awards, the estimated fair value is generally the fair market value of the underlying stock on the grant date. 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 No. 2016-09, *Compensation-Stock Compensation (Topic 718): Improvements to Employee Share-Based Payment Accounting* ("ASU 2016-09") effective January 1, 2017 and has elected to recognize forfeitures of stock-based awards as they occur on a prospective basis.

Net Loss per Share

Basic net loss per share is calculated by dividing the Company's net loss by the weighted average number of shares of common stock and Exchange Warrants outstanding during the period, without consideration of potentially dilutive securities. In accordance with Accounting Standards Codification Topic 260, *Earnings Per Share*, the Exchange Warrants are included in the computation of basic net loss per share because the exercise price is negligible and they are fully vested and exercisable after the original issuance date. Diluted net loss per share is the same as basic net loss per share for all periods presented since the effect of potentially dilutive securities is anti-dilutive given the net loss of the Company in each period. See Note 11. Stockholders' Equity for additional information regarding the Exchange Warrants.

Recently Issued Accounting Pronouncements Adopted During the Year Ended December 31, 2019

In February 2016, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") No. 2016-02, Leases (Topic 842). In July 2018, the FASB issued ASU No. 2018-10, Codification Improvements to Topic 842, *Leases*, which provides clarification to ASU 2016-02. These ASUs (collectively, the new lease standard) require an entity to recognize a lease liability and a ROU asset on the balance sheet for leases with lease terms of more than twelve months. Lessor accounting is largely unchanged, while lessees are no longer provided with a source of off-balance sheet financing. In July 2018, the FASB issued ASU No. 2018-11, *Leases* (Topic 842) - Targeted Improvements, which allows entities to elect an optional transition method where entities may continue to apply the existing lease guidance during the comparative periods and apply the new lease requirements through a cumulative effect adjustment in the period of adoption rather than in the earliest period presented. The Company adopted the new lease standard using the modified retrospective approach effective January 1, 2019 and elected the package of transitional practical expedients, such that, for leases existing prior to the adoption of ASC 842, the Company did not need to reassess whether contracts are leases, retained historical lease classification and historical initial direct costs classification. The Company did not elect the hindsight practical expedient to determine the lease term for existing leases. At January 1, 2019, the Company derecognized its deferred rent liability in the amount of $0.8 million and recognized a ROU asset and related lease liability in the amount of $7.5 million and $8.3 million, respectively.

In June 2018, the FASB issued ASU No. 2018-07, *Compensation – Stock Compensation (Topic 718), Improvements to Nonemployee Share-Based Payment Accounting*, which is intended to simplify the accounting for nonemployee share-based payment transactions by expanding the scope of Accounting Standards Codification Topic 718 – *Stock Compensation* ("ASC 718") include share-based payment transactions for acquiring goods and services from

nonemployees. The Company adopted this guidance prospectively as of January 1, 2019. The adoption of this guidance did not have a material impact on the Company's financial position, results of operations or liquidity.

Recently Issued Accounting Pronouncements Not Yet Adopted as of December 31, 2019

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 was originally effective for fiscal years and interim periods within those years beginning after December 15, 2019, with early adoption permitted for fiscal years and interim periods within those years beginning after December 15, 2018. In November 2019, the FASB issued ASU No. 2019-10, *Financial Instruments – Credit Losses (Topic 326), Derivatives and Hedging (Topic 815), and Leases (Topic 842): Effective Dates*, which amended the mandatory effective date of ASU No. 2016-13 to fiscal years and interim periods beginning after December 15, 2022. The Company is currently evaluating the impact of this new guidance on its consolidated financial statements and disclosures.

In August 2018, the FASB issued ASU No. 2018-13, *Fair Value Measurement (Topic 820) – Disclosure Framework – Changes to the Disclosure Requirements for Fair Value Measurement*, which modifies the disclosure requirements on fair value measurements and is intended to improve the effectiveness of disclosures, including the consideration of costs and benefits. The guidance is effective for the fiscal years and interim periods within those years beginning after January 1, 2020. Early adoption is permitted, and an entity is permitted to early adopt any removed or modified disclosures and delay adoption of additional disclosures until their effective date. The Company does not expect this new guidance to impact its consolidated financial statements and is currently evaluating the impact on its disclosures.

In November 2018, the FASB issued ASU No. 2018-18, *Collaborative Arrangements (Topic 808): Clarifying the Interaction Between Topic 808 and Topic 606*, which is intended to clarify the circumstances under which certain transactions in collaborative arrangements should be accounted for under the revenue recognition standard. Certain transactions between collaboration arrangement participants should be accounted for as revenue under ASC Topic 606 when the collaborative arrangement participant is a customer in the context of a unit of account. This guidance is effective for fiscal years and interim periods within those years beginning after December 15, 2020. Early adoption is permitted. The Company is in the process of assessing the impact of this new guidance on its consolidated financial statements and disclosures.

In December 2019, the FASB issued ASU No. 2019-12, *Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes,* which removes certain exceptions and amends certain requirements in the existing income tax guidance to ease accounting requirements. This guidance is effective for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2020 and must be applied on a retrospective basis. The Company is in the process of assessing the impact of this new guidance on its consolidated financial statements and disclosures.

Note 3. 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 (the "Janssen License and Collaboration Agreement") for the development, manufacture and potential 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 stockholder of the Company, and Janssen are both subsidiaries of Johnson & Johnson. PTG-200 is the Company's orally delivered gut-restricted 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 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 was responsible, at its own expense, for the conduct of the Phase 1 clinical trial for PTG-200, and Janssen is responsible for the conduct of the Phase 2 clinical trial for PTG-200 in CD, including filing the U.S. Investigational New Drug application ("IND"). Development costs for the Phase 2 clinical trial are shared between the parties on an 80/20 basis, with Janssen assuming the larger share. Janssen submitted an IND for PTG-200 in CD during the second quarter of 2019, which took effect in July 2019. The Company initiated a Phase 2 clinical study for PTG-200 in CD with Janssen in the fourth quarter of 2019.

The Company entered into an amendment (the "First Amendment") to the Janssen License and Collaboration Agreement effective May 7, 2019. The First Amendment builds upon the Company's ongoing development collaboration with Janssen for PTG-200 and, upon the effectiveness of the First Amendment, the Company became eligible to receive a $25.0 million payment from Janssen, which was received during the second quarter of 2019. The First Amendment expanded the scope of the Janssen License and Collaboration Agreement by supporting research efforts towards identifying and developing second-generation IL-23R antagonists ("second-generation compounds").

As part of the services added in the First Amendment, Janssen will pay certain costs and milestones related to advancing pre-clinical candidates from the second-generation research program through Phase 1 studies, including funding of a certain number of full-time equivalent employees ("FTEs") at the Company for a set period of time. The Company will pay 100% of the costs for the Phase 1 studies for the first second-generation compound, and 50% of the costs of the Phase 1 studies for the second and third second-generation compounds; thereafter Janssen will pay 100% of any further Phase 1 development costs. Development costs for the Phase 2 clinical trials for second-generation compounds are shared between the parties on an 80/20 basis, with Janssen assuming the larger share. The Company's Phase 1 and Phase 2 development costs are also limited by overall spending caps. In December 2019, the Company became eligible to receive a $5.0 million payment trigged by the successful nomination of a second-generation development compound. The Company will be eligible to receive a $7.5 million milestone payment at the completion of a Phase 1 study for the first second-generation compound.

Prior to the effectiveness of the First Amendment, the Company had been eligible to receive a $25.0 million milestone payment upon Janssen's filing of the IND. This amount had been considered constrained until a time at which the Company would have become eligible to receive the $25.0 million payment from Janssen. Payments to the Company for research and development services are generally billed and collected as services are performed or assets are delivered, including research activities and Phase 1 and Phase 2 development activities. Janssen bills the Company for its 20% share of the Phase 2 development costs as expenses are incurred by Janssen. Milestone payments are received after the related milestones are achieved.

Pursuant to the First Amendment, the Company will be eligible to receive clinical development, regulatory and sales milestones, if and as achieved, and/or payments relating to Janssen's elections to maintain or expand its license rights. The next such payment is a $50.0 million payment based on Phase 2a clinical trial results, as follows:

- Janssen can elect to advance PTG-200 into Phase 2b following receipt of the top line results of the CD Phase 2a clinical trial for PTG-200 by paying a $50.0 million maintenance fee (the "Amended First Opt-in Election"); or

- Janssen would make a $50.0 million milestone payment following dosing of the third patient in first Phase 2b clinical trial for CD for a second-generation product (the "Second-Generation Phase 2b Milestone").

Janssen can also then elect to receive exclusive, world-wide commercial rights for both PTG-200 and second-generation products following the Phase 2b completion date for PTG-200 or a second-generation product by paying a $50.0 million payment (the "Amended Second Opt-in Election"). Formerly, the first and second opt-in payments were $125.0 million and $200.0 million, respectively. If Janssen does not make the Amended Second Opt-in Election, with

respect to either PTG-200 or a second-generation compound, the Janssen License and Collaboration Agreement would terminate.

The Company will also be eligible for certain additional milestone payments including a potential payment of either $100.0 million upon a Phase 3 CD clinical trial meeting a primary clinical endpoint with respect to PTG-200 or $115.0 million upon a Phase 3 CD clinical trial meeting a primary clinical endpoint with respect to a second-generation compound.

Pursuant to the First Amendment, the Company will be eligible to receive tiered royalties on net product sales at percentages ranging from mid-single digits to ten percent. Under the terms of the First Amendment, the Company will be eligible to receive up to $1.0 billion in research, development, regulatory and sales milestones.

The Janssen License and Collaboration Agreement remains in effect until the royalty obligations cease following patent and regulatory expiry, unless terminated earlier. 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 has concluded that the amended Janssen License and Collaboration Agreement continues to contain a single performance obligation including the development license; second-generation compound research services; Phase 1 development services for PTG-200 and potential second-generation compounds; the Company's services associated with Phase 2 development for PTG-200 until Phase 2a; the Company's services associated with Phase 2 development for a second-generation product until the dosing of the third patient in Phase 2b; and all other such services that the Company may perform at the request of Janssen to support the development of PTG-200, second-generation research services, or the development of a second-generation compound. The Company concluded that the Amended First Opt-in Election and the Amended Second Opt-in Election options are not considered to be material rights.

The Company determined that the license was not distinct from the added research and development services within the context of the agreement because the added research and development services significantly increase the utility of the intellectual property. The Company also determined that the remaining research and development services are not distinct from the partially delivered combined promise comprised under the agreement prior to the First Amendment of the development license and PTG-200 services, including compound supply and other services. Therefore, the First Amendment is treated as if it were part of the original Janssen License and Collaboration Agreement. The First Amendment was accounted for as if it were an extension of services under the initial Janssen License and Collaboration Agreement by applying a cumulative catch-up adjustment to revenue. As of the effective date of the First Amendment, the Company calculated the adjusted cumulative revenue under the amended Janssen License and Collaboration Agreement by updating the transaction price for the incremental consideration to be received, net of the incremental development cost reimbursement to be paid to Janssen, and an updated percentage complete, which resulted in a cumulative adjustment recorded during the year ended December 31, 2019 that reduced revenue by $9.4 million.

The contract duration is defined as the period in which parties to the contract have present enforceable rights and obligations. For revenue recognition purposes, the Company determined that the duration of the Janssen License and Collaboration Agreement, as amended, began on the effective date of July 13, 2017 and ends upon the later of end of Phase 2a for PTG-200 or upon dosing of the third patient in Phase 2b for a second-generation compound.

The Company uses the most likely amount method to estimate variable consideration included in the transaction price. Variable consideration after the First Amendment consists of future milestone payments and cost sharing payments from Janssen for agreed upon services offset by Phase 2 development costs reimbursement payable to Janssen. Cost sharing payments from Janssen relate to the 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.

Cost sharing payments to Janssen relate to agreed upon services for Phase 2 activities that Janssen performs within the duration of the contract 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 determined that the transaction price of the Janssen License and Collaboration Agreement was $112.9 million as of December 31, 2019, an increase of $52.2 million from the transaction price of $60.7 million at December 31, 2018 and $59.0 million from the transaction price of $53.9 million at December 31, 2017. In order to determine the transaction price, the Company evaluated all payments to be received during the duration of the contract, net of Phase 2 development costs reimbursement expected to be payable to Janssen. The Company determined that the transaction price includes the $50.0 million upfront payment, the $25.0 million payment received upon the effectiveness of the First Amendment, the $5.0 million payment triggered by the successful nomination of a second-generation compound, $18.3 million of reimbursement from Janssen for services performed for PTG-200 Phase 2 and for second-generation compound research costs and other services, and $14.6 million of estimated variable consideration, which includes a $7.5 million milestone payment subject to the completion of a Phase 1 study for a second-generation compound. The Company evaluated whether the variable component of the transaction price should be constrained to ensure that a significant reversal of revenue recognized on a cumulative basis as of December 31, 2019 is not probable. The Company concluded that the variable consideration constraint does not further decrease the estimated transaction price as of December 31, 2019. The additional potential development, regulatory and sales milestone payments after the completion of Phase 2b activities that the Company would be eligible to receive are currently outside the contract term as defined for revenue recognition purposes and as such have been excluded from the transaction price. The increase in transaction price following the effectiveness of the First Amendment was primarily due to the collection of the $25.0 million payment, the $5.0 million payment receivable as of December 31, 2019, the $7.5 million milestone payment for the successful completion of a Phase 1 study for a second- generation compound and increases in reimbursable costs related to new and extended research and development services, offset by Phase 2 development costs reimbursement payable to Janssen.

The Company re-evaluates the transaction price, including variable consideration, at the end of each reporting period and as uncertain events are resolved or other changes in circumstances occur. 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 utilizes a cost-based input method to measure proportional performance and to calculate the corresponding amount of revenue to recognize. In applying the cost-based input methods of revenue recognition, the Company uses actual costs incurred relative to expected costs to fulfill the combined performance obligation. These costs consist primarily of internal FTE effort and third-party contract costs. Revenue will be recognized based on actual costs incurred as a percentage of total estimated costs as the Company completes its performance obligations. A cost-based input method of revenue recognition requires management to make estimates of costs to complete the Company's performance obligations. 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 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, 2019, the Company recognized $0.2 million of license and collaboration revenue. This amount included a $9.4 million cumulative catchup adjustment as a reduction of revenue, offset by $8.0 million of license and collaboration revenue recognized following the contract modification for the First Amendment and $1.6 million of collaboration revenue recognized during the first quarter of 2019 under the original Janssen License and Collaboration Agreement prior to the effectiveness of the First Amendment.

For the year ended December 31, 2018, the Company recognized $30.9 million of license and collaboration revenue. This amount included $30.8 million of the transaction price for the Janssen License and Collaboration Agreement recognized based on proportional performance, and $0.1 million, net, for other services related to Phase 2

activities performed by the Company on behalf of Janssen that were not included in the performance obligations identified under the Janssen License and Collaboration Agreement.

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 were 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 years ended December 31, 2019 and 2018 (in thousands):

Year Ended December 31, 2019	Balance at Beginning of Period	Additions	Deductions	Balance at End of Period
Contract assets:				
Receivable from collaboration partner - related party	$ 2,042	$ 36,837	$ (32,924)	$ 5,955
Contract asset - related party	$ 2,545	$ 800	$ (2,545)	$ 800
Contract liabilities:				
Deferred revenue - related party	$ 8,223	$ 42,456	$ (9,149)	$ 41,530
Payable to collaboration partner - related party	$ 1,061	$ 1,468	$ (1,267)	$ 1,262

Year ended December 31, 2018	Balance at Beginning of Period	Additions	Deductions	Balance at End of Period
Contract assets:				
Receivable from collaboration partner - related party	$ 1,816	$ 6,665	$ (6,439)	$ 2,042
Contract asset - related party	$ —	$ 2,545	$ —	$ 2,545
Contract liabilities:				
Deferred revenue - related party	$ 31,752	$ 7,296	$ (30,825)	$ 8,223
Payable to collaboration partner - related party	$ —	$ 1,574	$ (513)	$ 1,061

During the year ended December 31, 2019, the Company recognized $1.6 million in revenue from the deferred revenue contract liability balance at the beginning of the year, which represents the revenue recognized during the first quarter of 2019 prior to the effectiveness of the First Amendment. During the year ended December 31, 2018, the Company recognized $23.5 million in revenue from the deferred revenue contract liability balance at the beginning of the year. 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 year 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, 2019			
	Level 1	Level 2	Level 3	Total
Assets:				
Money market funds	$ 12,964	$ —	$ —	$ 12,964
Commercial paper	—	44,282	—	44,282
Corporate debt securities	—	33,662	—	33,662
U.S. Treasury and agency securities	—	40,810	—	40,810
Total financial assets	$ 12,964	$ 118,754	$ —	$ 131,718

	December 31, 2018			
	Level 1	Level 2	Level 3	Total
Assets:				
Money market funds	$ 25,390	$ —	$ —	$ 25,390
Commercial paper	—	59,730	—	59,730
Corporate debt securities	—	8,989	—	8,989
U.S. Treasury and agency securities	—	33,394	—	33,394
Total financial assets	$ 25,390	$ 102,113	$ —	$ 127,503

The Company's commercial paper, corporate debt securities and U.S. Treasury and agency securities 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.

Fair Value of Other Financial Instruments

The carrying value of long-term debt approximates fair value because the Term Loan bears interest at a rate that approximates prevailing market rates for instruments with similar characteristics and there is no significant change in the credit worthiness of the Company.

Note 5. Balance Sheet Components

Cash Equivalents and Marketable Securities

Cash equivalents and marketable securities consisted of the following (in thousands):

	December 31, 2019			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Money market funds	$ 12,964	$ —	$ —	$ 12,964
Commercial paper	44,284	2	(4)	44,282
Corporate debt securities	33,653	11	(2)	33,662
U.S. Treasury and agency securities	40,798	14	(2)	40,810
Total cash equivalents and marketable securities	$ 131,699	$ 27	$ (8)	$ 131,718
Classified as:				
Cash equivalents				$ 31,707
Marketable securities				100,011
Total cash equivalents and marketable securities				$ 131,718

	December 31, 2018			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Money market funds	$ 25,390	$ —	$ —	$ 25,390
Commercial paper	59,730	—	—	59,730
Corporate debt securities	8,997	—	(8)	8,989
U.S. Treasury and agency securities	33,423	—	(29)	33,394
Total cash equivalents and marketable securities	$ 127,540	$ —	$ (37)	$ 127,503
Classified as:				
Cash equivalents				$ 80,883
Marketable securities				46,620
Total cash equivalents and marketable securities				$ 127,503

All marketable securities held as of December 31, 2019 and 2018 had contractual maturities of less than one year. There were no material realized gains or realized losses from sales of marketable 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,	
	2019	2018
Prepaid clinical and research related expenses	$ 2,567	$ 686
Prepaid insurance	1,161	438
Other prepaid expenses	1,057	1,005
Other receivable	744	495
Prepaid expenses and other current assets	$ 5,529	$ 2,624

Property and Equipment, Net

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

	December 31,	
	2019	2018
Laboratory equipment	$ 2,947	$ 2,533
Furniture and computer equipment	512	338
Leasehold improvements	863	67
Total property and equipment	4,322	2,938
Less: accumulated depreciation and amortization	(2,641)	(2,077)
Property and equipment, net	$ 1,681	$ 861

Depreciation expense for the years ended December 31, 2019, 2018, and 2017 was $703,000, $527,000 and $406,000, respectively. As of December 31, 2019, 2018 and 2017, $37,000, $200 and $1,200, 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,	
	2019	2018
Accrued clinical and research related expenses	$ 7,232	$ 7,781
Accrued employee related expenses	4,637	2,726
Accrued professional service fees	301	61
Accrued interest payable	68	—
Other	122	595
Total accrued expenses and other payables	$ 12,360	$ 11,163

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 that relates to the products arising from the collaboration. 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 former collaboration partner could be eligible to receive up to an additional aggregate of $128.0 million for the achievement of certain development, regulatory and sales milestone events. Milestone payments to collaboration partners are recorded as research and development expenses in the period that the expense is incurred. No research and development expense was recorded under this agreement for the year ended December 31, 2019. For the years ended December 31, 2018 and 2017, the Company recorded research and development expense of $500,000 and $250,000, respectively, under this agreement.

Note 7. Government Programs

Research and Development Tax Incentive

The Company recognized AUD 1.9 million ($1.3 million) of research and development expenses during the year ended December 31, 2019 in connection with a reversal of previously recorded reductions to research and development expenses related to the research and development tax incentive from the ATO. The Company determined that it had exceeded the annual turnover limit to claim such amounts following the receipt of certain payments under the Janssen License and Collaboration Agreement. The Company is eligible to apply for the taxable credit in the form of a non-cash

tax incentive from the ATO for the year ended December 31, 2019. For the years ended December 31, 2018 and 2017, the Company recognized AUD 2.1 million ($1.6 million) and AUD 1.7 million ($1.3 million), respectively, as a reduction of research and development expenses in connection with the research and development cash tax incentive from the ATO. As of December 31, 2018, the research and development tax incentive receivable was AUD 2.0 million ($1.4 million). There was no research and development tax incentive receivable as of December 31, 2019.

SBIR Grant

In July 2016, the Company was awarded a Phase 1 SBIR grant from the National Heart, Lungs and Blood Institute ("NHLBI") of the NIH in support of pre-clinical 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 May 2017, the Company was awarded a Phase 2 SBIR grant from the National Institute of Diabetes and Digestive and Kidney Diseases of the NIH in support of research aimed at developing biomarkers that define IL-23R target engagement by orally delivered peptide antagonists and the effects of that engagement of downstream signaling. The total grant award was $1.3 million and was originally for the period from May 2017 to April 2019. During the year ended December 31, 2019, the Company requested and received an extension of this grant through April 2020.

In September 2018, the Company was awarded a Phase 2 SBIR Grant from the NHLBI of the NIH in support of research aimed at developing the Company's novel hepcidin mimetic PTG-300 for the potential treatment of chronic anemia and iron overload in rare blood disorders, including beta-thalassemia. The total grant award was $1.5 million and is for the period from September 2018 to August 2020.

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 $1.4 million, $663,000 and $182,000 as a reduction of research and development expenses for the years ended December 31, 2019, 2018 and 2017, respectively. The Company recorded a receivable for $304,000 and $309,000 as of December 31, 2019 and 2018, respectively, to reflect the eligible costs incurred under the grants that are contractually due to the Company. This receivable is included in prepaid expenses and other current assets on the consolidated balance sheets.

Note 8. Debt

On October 30, 2019, the Company entered into a Credit and Security Agreement, dated as of October 30, 2019 (the "Closing Date") by and among the Company, MidCap Financial Trust, as a lender, Silicon Valley Bank, as a lender, the other lenders party thereto from time to time and MidCap Financial Trust, as administrative agent and collateral agent ("Agent") (the "Term Loan Credit Agreement"), which provides for a $50.0 million term loan facility. The Term Loan Credit Agreement provides for (i) on the Closing Date, $10.0 million aggregate principal amount of term loans, (ii) at the Company's option, until December 31, 2020, an additional $20.0 million term loan facility subject to the satisfaction of certain conditions, including clinical milestone achievement, and (iii) at the Company's option, until September 30, 2021, an additional $20.0 million term loan facility subject to the satisfaction of certain conditions, including clinical milestone achievement, (collectively, the "Term Loans"). The Company intends to use the proceeds of the Term Loans for general corporate purposes

The Term Loans are subject to an origination fee of 0.25% for each funded tranche under the Term Loan Credit Agreement and bear interest at an annual rate based on prime rate plus 2.91%, subject to a prime rate floor of 4.94%. The Company will make interest-only payments on the Term Loans for 24 months, followed by 24 months of principal and interest payments. At the Company's option, the Company may prepay the outstanding principal balance of the Term Loans in whole or in part, subject to a prepayment premium of 3.0% of any amount prepaid if the prepayment occurs through and including the first anniversary of the closing date, 2.0% of the amount prepaid if the prepayment occurs after the first anniversary of the closing date through and including the second anniversary of the closing date, and 1.0% of any amount prepaid after the second anniversary of the closing date and prior to October 1, 2023. An additional fee of 2.85% of the amount of Term Loans advanced by the Lenders will be due upon prepayment or repayment of the Term Loans.

The Term Loan Credit Agreement requires the Company to maintain cash and cash equivalents of at least 35% of the outstanding Term Loans at all times and is secured by a perfected security interest in all of the Company's assets except for intellectual property and certain other customary excluded property pursuant to the terms of the Term Loan Credit Agreement. The Term Loan Credit Agreement contains other covenants that limit the Company's ability and the ability of its subsidiaries to perform certain actions, including obligations to not pay dividends and to maintain unrestricted cash balance above certain threshold, non-occurrence of material adverse change, non-occurrence of change of control and other customary affirmative and negative covenants. The violation of any provision of covenants will result in default for the Company. The Term Loan Credit Agreement includes a clause which allows lenders to accelerate repayment upon the occurrence of certain events of default. As of December 31, 2019, the Company was in compliance with the debt covenants, no event of default occurred and the probability of occurrence of event of default was considered remote.

As of December 31, 2019, the Company's long-term debt balance was as follows (dollars in thousands):

	Maturity Date	Annual Interest Rate	December 31, 2019
Term loan	10/1/2023	7.85%	$ 10,000
Debt issuance costs, net of amortization			(222)
Accrued final payment fee			16
Long-term debt, net			$ 9,794

The Company incurred $235,000 of issuance costs related to the Term Loan. As of December 31, 2019, the carrying value of debt issuance costs was $222,000 and was presented as a direct deduction from the carrying amount of long-term debt. For the year ended December 31, 2019, $13,000 of debt issuance costs were amortized and recognized as interest expense in the statement of operations. In addition, $16,000 of accreted final payment fees were recognized as interest expense in the statement of operations and included in the carrying amount of long-term debt for the year ended December 31, 2019. The effective interest rate on long-term debt was 9.81% for the year ended December 31, 2019.

The following table summarizes the Company's minimum future debt payment obligations including principal and final payment fee as of December 31, 2019 (in thousands):

Year Ending December 31:	Amount
2020	$ —
2021	833
2022	5,000
2023	4,452
Total	$ 10,285

Note 9. Leases

On January 1, 2019, the Company adopted ASC 842, which requires entities to recognize assets and liabilities for leases with lease terms of more than 12 months on the balance sheet. Adoption of ASC 842 resulted in the recording of operating lease assets of $7.5 million and operating lease liabilities of $8.3 million. The impact of the changes made

to the consolidated balance sheet as of January 1, 2019 as a result of adopting the new guidance was as follows (in thousands):

	Balance at December 31, 2018	Adjustments Due to ASC 842	Balance at January 1, 2019
Balance Sheet:			
Operating lease right-of-use asset - noncurrent	$ —	7,499	$ 7,499
Operating lease liability - current	$ —	1,080	$ 1,080
Operating lease liability - noncurrent	$ —	7,219	$ 7,219
Deferred rent - noncurrent	$ 799	(799)	$ —

The Company has one operating lease agreement entered into in March 2017 for laboratory and office space located in Newark, California. 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. During 2019, the Company received $469,000 from the landlord for eligible leasehold improvements made to the leased property. Leases with terms of 12 months or less are not recorded on the balance sheet, and the related lease expenses are recognized on a straight-line basis over the lease term. During the year ended December 31, 2019, the Company recognized $64,000 of sublease income. The Company did not recognize any sublease income for the years ended December 31, 2018 and 2017. Under the terms of the lease, we are responsible for certain taxes, insurance and maintenance expenses.

The weighted average lease term and discount rate are as follows:

	December 31, 2019
Operating Lease Term and Discount Rate:	
Weighted-average remaining lease term	4.4 years
Weighted-average discount rate	11.0%

The following table summarizes the Company's minimum lease payments and lease liability as of December 31, 2019 (in thousands):

Year Ending December 31:	Amount
2020	$ 1,941
2021	2,000
2022	2,059
2023	2,121
2024	895
Thereafter	—
Total future minimum lease payments	9,016
Less: imputed interest	(1,799)
Present value of future minimum lease payments	7,217
Less: current portion of operating lease liability	(1,256)
Operating lease liability - noncurrent	$ 5,961

As previously disclosed in the Company's 2018 Annual Report on Form 10-K and under the previous lease accounting standard, future minimum operating leases having initial or remaining noncancelable lease terms in excess of one year would have been as follows (in thousands):

Year Ending December 31:	Amount
2019	$ 1,941
2020	2,000
2021	2,059
2022	2,121
2023	2,185
Thereafter	922
Total	$ 11,228

Supplemental lease cost information is as follows (in thousands):

	Year Ended December 31, 2019
Operating lease cost	$ 1,792

Supplemental balance sheet information is as follows (in thousands):

	December 31, 2019
Operating Leases:	
Operating lease right-of-use asset, non-current	$ 6,042
Operating lease liability - current	$ 1,256
Operating lease liability - noncurrent	5,961
Total operating lease liabilities	$ 7,217

Supplemental cash flow information is as follows (in thousands):

	Year Ended December 31, 2019
Cash paid for amounts included in the measurement of lease liabilities:	
Operating cash flow used by operating leases	$ 1,885

Prior to the adoption of ASC 842, the Company's rent expense was $1.9 million and $1.4 million for the years ended December 31, 2018 and 2017, respectively. Rent expense was recognized on a straight-line basis over the term of the lease and accordingly, the Company recorded the difference between cash rent payments and the recognition of rent expense as a deferred rent liability.

Note 10. Commitments and Contingencies

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 carries a directors' and officers' insurance policy. 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 11. Stockholders' Equity

In September 2017, the Company filed a registration statement on Form S-3 with the Securities and Exchange Commission (File No. 333-220314) that was declared effective as of October 5, 2017 and 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, preferred stock and certain debt securities (the "2017 Form S-3"). 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 ("ATM") financing facility under a sales agreement (the "2017 Sales Agreement"). The 2017 Sales Agreement was terminated in 2019. During the year ended December 31, 2019, prior to the termination of the 2017 Sales Agreement, the Company sold 2,846,641 shares of its common stock for net proceeds of $34.5 million, after deducting issuance costs. The Company sold 151,273 shares of its common stock pursuant to the 2017 Sales Agreement during the year ended December 31, 2018 for net proceeds of $1.5 million, after deducting issuance costs. As of December 31, 2019, $72.0 million of common stock remained available for sale under the 2017 Form S-3.

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.

In August 2018, the Company entered into a Securities Purchase Agreement with certain accredited investors (each, an "Investor" and, collectively, the "Investors"), pursuant to which the Company sold an aggregate of 2,750,000 shares of its common stock at a price of $8.00 per share, for aggregate net proceeds of $21.7 million, after deducting offering expenses payable by the Company. In a concurrent private placement, the Company issued the Investors warrants to purchase an aggregate of 2,750,000 shares of its common stock (each, a "Warrant" and, collectively, the "Warrants"). Each Warrant is exercisable from August 8, 2018 through August 8, 2023. Warrants to purchase 1,375,000 shares of the Company's common stock have an exercise price of $10.00 per share and Warrants to purchase 1,375,000 shares of the Company's common stock have an exercise price of $15.00 per share. The exercise price and number of shares of common stock issuable upon the exercise of the Warrants (the "Warrant Shares") are subject to adjustment in the event of any stock dividends and splits, reverse stock split, recapitalization, reorganization or similar transaction, as described in the Warrants. Under certain circumstances, the Warrants may be exercisable on a "cashless" basis. In connection with the issuance and sale of the common stock and Warrants, the Company granted the Investors certain registration rights with respect to the Warrants and the Warrant Shares. The common stock and warrants are classified as equity in accordance with Accounting Standards Codification Topic 480*, Distinguishing Liabilities from Equity* ("ASC 480")*,* and the net proceeds from the transaction were recorded as a credit to additional paid-in capital. As of December 31, 2019, none of the Warrants have been exercised.

In December 2018, the Company entered into an exchange agreement (the "Exchange Agreement") with an Investor and its affiliates (the "Exchanging Stockholders"), pursuant to which the Company exchanged an aggregate of 1,000,000 shares of the Company's common stock, par value $0.00001 per share, owned by the Exchanging Stockholders for pre-funded warrants (the "Exchange Warrants") to purchase an aggregate of 1,000,000 shares of common stock (subject to adjustment in the event of any stock dividends and splits, reverse stock split, recapitalization, reorganization or similar transaction, as described in the Exchange Warrants), with an exercise price of $0.00001 per share. The Exchange Warrants will expire ten years from the date of issuance. The Exchange Warrants are exercisable at any time prior to expiration except that the Exchange Warrants cannot be exercised by the Exchanging Stockholders if, after giving effect thereto, the Exchanging Stockholders would beneficially own more than 9.99% of the Company's common stock, subject to certain exceptions. In accordance with Accounting Standards Codification Topic 505, *Equity* , the Company recorded the retirement of the common stock exchanged as a reduction of common stock shares outstanding and a corresponding debit to additional paid-in-capital at the fair value of the Exchange Warrants on

the issuance date. The Exchange Warrants are classified as equity in accordance with ASC 480, and fair value of the Exchange Warrants was recorded as a credit to additional paid-in capital and is not subject to remeasurement. The Company determined that the fair value of the Exchange Warrants is substantially similar to the fair value of the retired shares on the issuance date due to the negligible exercise price for the Exchange Warrants. During the year ended December 31, 2019, Exchange Warrants to purchase 600,000 shares were net exercised, resulting in the issuance of 599,997 shares of common stock. As of December 31, 2019, 400,000 of the Exchange Warrants remain unexercised.

In October 2019, the Company filed a registration statement on Form S-3 (File no. 333-234414) that was declared effective as of November 22, 2019 and permits the offering, issuance, and sale by the Company of up to a maximum aggregate offering price of $250.0 million of its common stock, preferred stock, debt securities and warrants (the "2019 Form S-3"). Up to a maximum of $75.0 million of the maximum aggregate offering price of $250.0 million may be issued and sold pursuant to an ATM financing facility under a sales agreement entered into by the Company on November 27, 2019 (the "2019 Sales Agreement"). As of December 31, 2019, no offering, issuance or sale of common stock, preferred stock, debt securities or warrants was made under the 2019 Form S-3 or the 2019 Sales Agreement.

Note 12. 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. 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, 2019, approximately 602,091 shares of common stock were available 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.

Inducement Plan

In May 2018, the Company's board of directors approved the 2018 Inducement Plan, a non-stockholder approved stock plan, under which it reserved and authorized 750,000 shares of the Company's common stock in order to award options and restricted stock unit awards to persons that were not previously employees or directors of the Company, or following a bona fide period of non-employment, as an inducement material to such persons entering into employment with the Company, within the meaning of Rule 5635(c)(4) of the Nasdaq Listing Rules. The 2018 Inducement Plan is administered by the board of directors or the Compensation Committee of the board, 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. Awards granted under the 2018 Inducement Plan expire no later than ten years from the date of grant. As of December 31, 2019, approximately 280,000 shares were available for issuance under the 2018 Inducement Plan.

Stock Options

Activity under the Company's equity incentive plans is set forth below:

	Options Outstanding	Weighted-Average Exercise Price Per Share	Weighted-Average Remaining Contractual Life (years)	Aggregate Intrinsic Value (1) (in millions)
Balances at December 31, 2018	3,178,441	$ 12.23	7.52	
Options granted	1,328,800	9.36		
Options exercised	(307,055)	3.81		
Options forfeited	(518,665)	14.08		
Balances at December 31, 2019	3,681,521	$ 11.64	7.78	$ 2.4
Options exercisable – December 31, 2019	1,973,866	$ 11.82	6.93	$ 2.3
Options vested and expected to vest – December 31, 2019	3,681,521	$ 11.64	7.78	$ 2.4

(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, 2019. The calculation excludes options with an exercise price higher than the closing price of the Company's common stock on December 31, 2019.

The aggregate intrinsic value of options exercised was $2.6 million, $1.3 million and $3.5 million for the years ended December 31, 2019, 2018 and 2017, respectively.

During the years ended December 31, 2019, 2018 and 2017, the estimated weighted-average grant-date fair value of common stock underlying options granted was $5.45, $8.12 and $7.74 per share, respectively.

Stock Options Valuation

The fair value of stock option awards accounted for under ASC 718 was estimated at the date of grant using a Black-Scholes option-pricing model with the following assumptions:

	Year Ended December 31,		
	2019	2018	2017
Expected term (in years)	5.00 - 6.08	5.49 - 6.08	5.50 - 6.08
Expected volatility	61.0% - 64.8%	62.0% - 66.5%	61.6% - 65.4%
Risk-free interest rate	1.42% - 2.58%	2.42% - 3.03%	1.88% - 2.24%
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 expected volatility 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 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.

Restricted Stock Units

The Company began issuing restricted stock units under the 2016 Plan during the year ended December 31, 2018. A restricted stock unit is an agreement to issue shares of the Company's common stock at the time of vesting. Restricted stock unit annual refresher awards vest in four equal installments on approximately the first, second, third and fourth anniversaries of the grant date. Restricted stock unit incentive awards granted during 2018 vest in three equal installments at six months intervals over a period of 18 months.

Restricted stock unit activity under the Company's equity incentive plans is set forth below:

	Number of Shares	Weighted Average Grant Date Fair Value
Unvested at December 31, 2018	418,450	$ 10.45
Restricted grant units granted	160,650	8.02
Restricted grant units vested	(197,703)	9.29
Restricted grant units forfeited	(102,915)	9.88
Unvested at December 31, 2019	278,482	$ 10.08

Stock-based compensation expense associated with restricted stock units is based on the fair value of the Company's common stock on the grant date, which equals the closing market price of the Company's common stock on the grant date. For restricted stock units, the Company recognizes compensation expense over the vesting period of the awards that are ultimately expected to vest.

Employee Stock Purchase Plan

In July 2016, the Company's board of directors and stockholders approved the 2016 Employee Stock Purchase Plan ("2016 ESPP"). 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. During the year ended December 31, 2019, 79,034 shares were issued under the ESPP. As of December 31, 2019, 577,993 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,		
	2019	2018	2017
Expected term (in years)	0.50	0.50	0.50
Expected volatility	58.9% -65.3%	49.0% -63.4%	52.4%
Risk-free interest rate	1.89% -2.32%	1.89% -2.32%	0.89% - 1.16%
Dividend yield	—	—	—

Stock-Based Compensation

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

	Year Ended December 31,		
	2019	2018	2017
Research and development	$ 4,350	$ 3,424	$ 2,008
General and administrative	4,003	3,495	2,233
Total stock-based compensation expense	$ 8,353	$ 6,919	$ 4,241

As of December 31, 2019, total unrecognized stock-based compensation expense was $12.3 million, which the Company expects to recognize over a period of approximately 2.5 years.

Note 13. 401(k) Plan

The Company has a retirement and savings plan under Section of 401(k) of Internal Revenue Code (the "401(k) Plan") covering all U.S. employees. The 401(k) Plan allows employees to make pre- and post-tax contributions up to the maximum allowable amount set by the Internal Revenue Service. The Company does not make matching contributions to the 401(k) Plan on behalf of participants.

Note 14. Income Taxes

The Company recorded an income tax benefit of $0.7 million for the year ended December 31, 2019 primarily due to research and development tax credits and the recognition of deferred tax assets in Protagonist Australia. The Company believes these deferred tax assets will be realized in the future due to expected profitability for this subsidiary.

The Company recorded an income tax benefit of $0.8 million for the year ended December 31, 2018 from the recognition of deferred tax assets in Protagonist Australia. No provision for income taxes was recorded for the year ended December 31, 2017. The Company had incurred net operating losses and did not reflect any benefit of operating loss carryforwards in the consolidated financial statements for the year ended December 31, 2017. The Company continues to maintain a valuation allowance against its U.S. deferred tax assets due to the uncertainty surrounding the realization of such assets.

The following table presents domestic and foreign components of net loss before income taxes (in thousands):

	Year Ended December 31,		
	2019	2018	2017
Domestic	$ (72,271)	$ (37,511)	$ (34,556)
Foreign	(5,607)	(2,212)	(2,401)
Total net loss before taxes	$ (77,878)	$ (39,723)	$ (36,957)

The federal, state and foreign components of the income tax expense (benefit) are summarized as follows:

	Year Ended December 31,		
	2019	2018	2017
Current:			
Federal	$ —	$ —	$ —
State	—	—	—
Foreign	84	—	—
Total current tax expense	84	—	—
Deferred:			
Federal	—	—	—
State	—	—	—
Foreign	(775)	(799)	—
Total deferred tax benefit	(775)	(799)	—
Income tax benefit	$ (691)	$ (799)	$ —

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

	Year Ended December 31,		
	2019	2018	2017
Federal statutory income tax rate	21.0 %	21.0 %	34.0 %
State taxes, net of federal benefit	1.2	7.0	0.5
Research and development credits	4.3	(1.3)	2.6
Foreign tax rate difference	0.7	0.4	(1.2)
Change in valuation allowance	(23.8)	(22.2)	(5.2)
Change in tax law	—	—	(31.2)
Other	(2.5)	(2.9)	0.5
Provision for income taxes	0.9 %	2.0 %	— %

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

	December 31,	
	2019	2018
Deferred tax assets:		
Net operating loss carryforwards	$ 39,907	$ 27,704
Depreciation and amortization	318	269
Accruals/other	5,454	2,455
Operating lease liability	1,516	—
Research and development credits	8,038	4,270
Total deferred tax assets	55,233	34,698
Deferred tax liabilities:		
Operating right-of-use asset	(1,269)	—
Total deferred tax liabilities	(1,269)	—
Valuation allowance	(52,531)	(34,040)
Net deferred tax assets	$ 1,433	$ 658

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 U.S. deferred tax assets as of December 31, 2019 and 2018 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 $18.5 million, $8.2 million and $1.9 million during the years ended December 31, 2019, 2018 and 2017, respectively.

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 certain of its equity financing transactions.

At December 31, 2019, the Company had $164.1 million of federal net operating loss carryforwards and $151.1 million of state net operating loss carryforwards. $78.7 million of the federal net operating loss carryforwards will begin to expire in 2033, if not utilized, and the remaining $85.4 million have no expiration. The state net operating loss carryforwards will begin to expire in 2035, if not utilized.

At December 31, 2019, the Company also had accumulated Australian tax losses of AUD 13.1 million ($9.2 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, 2019, the Company had $6.6 million of federal and $3.3 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.

As of December 31, 2019, the Company had AUD 3.5 million ($2.5 million) of Australian research and development tax credit carryforwards available to reduce future income taxes. The Australian research and development tax credits have no expiration date.

A reconciliation of the beginning and ending amount of unrecognized tax benefits is as follows (in thousands):

	Year Ended December 31,		
	2019	2018	2017
Balance at beginning of year	$ 9,466	$ 5,414	$ 2,131
Increase based on tax positions related to prior years	184	108	—
Increase based on tax positions related to current year	6,981	3,944	3,283
Balance at end of year	$ 16,631	$ 9,466	$ 5,414

At December 31, 2019, the Company had unrecognized tax benefits of $16.6 million, of which $4.1 million would affect the effective tax rate if recognized and $12.5 million is subject to a valuation allowance and would not affect the effective tax rate if recognized. The Company does not anticipate that the total amounts of unrecognized tax benefits will significantly increase or decrease in the next 12 months. The Company's policy is to include interest and penalties related to unrecognized tax benefits within the provision for income taxes, as necessary. Management determined that no accrual for interest or penalties was required as of December 31, 2019, 2018 and 2017.

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 remain open for examination for all years.

Note 15. Net Loss per Share

As the Company had net losses for the years ended December 31, 2019, 2018 and 2017, 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 (in thousands, except share and per share data):

	Year Ended December 31,		
	2019	2018	2017
Numerator:			
Net loss	$ (77,187)	$ (38,924)	$ (36,957)
Denominator:			
Weighted-average shares used to compute net loss per common share, basic and diluted	25,894,024	22,364,515	17,694,505
Net loss per shares, basic and diluted	$ (2.98)	$ (1.74)	$ (2.09)

The following outstanding shares of potentially dilutive securities have been excluded from diluted net loss per share calculations for the years ended December 31, 2019, 2018 and 2017 because their inclusion would be anti-dilutive:

	Year Ended December 31,		
	2019	2018	2017
Options to purchase common stock	3,681,521	3,178,441	2,438,151
Common stock warrants	2,750,000	2,750,000	—
Restricted stock units	278,482	418,450	—
ESPP shares	40,275	52,134	24,938
Total	6,750,278	6,399,025	2,463,089

Note 16. Supplementary Financial Data (unaudited)

The following table presents the selected quarterly financial data for the years ended December 31, 2019 and 2018 (in thousands, except per share amounts):

	Consolidated Statements of Operations			
	Quarter Ended			
	March 31	June 30	September 30	December 31
2019				
License and collaboration revenue - related party	$ 1,560	$ (8,189)	$ 4,141	$ 2,719
Loss from operations	$ (14,648)	$ (31,407)	$ (17,167)	$ (17,299)
Net loss	$ (14,103)	$ (29,174)	$ (16,409)	$ (17,501)
Net loss per share of common stock, basic and diluted [(1)]	$ (0.58)	$ (1.18)	$ (0.61)	$ (0.63)
2018				
License and collaboration revenue - related party	$ 10,781	$ 11,674	$ 6,117	$ 2,353
Loss from operations	$ (8,229)	$ (9,239)	$ (9,389)	$ (15,412)
Net loss	$ (7,661)	$ (8,663)	$ (8,735)	$ (13,865)
Net loss per share of common stock, basic and diluted [(1)]	$ (0.36)	$ (0.41)	$ (0.38)	$ (0.57)

[(1)] Net loss per share amounts for the 2019 and 2018 quarters and full years have been computed separately. Accordingly, quarterly amounts may not add to the annual amounts because of differences in the weighted average shares outstanding during each period.

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 (Principal Executive Officer) and Chief Financial Officer (Principal 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, 2019. 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, 2019 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, 2019.

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.

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 2020 Annual Meeting of Stockholders within 120 days after the end of the fiscal year ended December 31, 2019.

We have adopted a Code of Business Conduct and Ethics that applies to all 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 2020 Annual Meeting of Stockholders within 120 days after the end of the fiscal year ended December 31, 2019.

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 2020 Annual Meeting of Stockholders within 120 days after the end of the fiscal year ended December 31, 2019.

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 2020 Annual Meeting of Stockholders within 120 days after the end of the fiscal year ended December 31, 2019.

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 2020 Annual Meeting of Stockholders within 120 days after the end of the fiscal year ended December 31, 2019.

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	001-37852	3.1	8/16/2016	
3.2	Amended and Restated Bylaws	S-1/A	333-212476	3.2	8/1/2016	
4.1	Specimen stock certificate evidencing the shares of common stock	S-1/A	333-212476	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	333-212476	4.2	8/1/2016	
4.3	Form of Indenture	S-3	333-220314	4.5	9/1/2017	
4.4	Form of Class A Common Stock Purchase Warrant	8-K	001-37852	4.1	8/7/2018	
4.5	Form of Class B Common Stock Purchase Warrant	8-K	001-37852	4.2	8/7/2018	
4.6	Form of Warrant	8-K	001-37852	4.1	12/31/2018	
4.7	Description of Protagonist Therapeutics, Inc.'s Securities Registered Pursuant to Section 12 of the Exchange Act					X
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	333-212476	10.1	7/11/2016	

Exhibit Number	Exhibit Description	Incorporation By Reference				Filed Herewith
		Form	SEC File No.	Exhibit	Filing Date	
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	333-212476	10.2	8/1/2016	
10.3+	Protagonist Therapeutics, Inc. 2016 Employee Stock Purchase Plan.	S-1/A	333-212476	10.3	8/1/2016	
10.4+	Form of Indemnity Agreement for Directors and Officers.	S-1/A	333-212476	10.4	8/1/2016	
10.5+	Protagonist Therapeutics, Inc. 2018 Inducement Plan, form of stock option grant notice, form of option agreement, form of restricted stock unit grant notice and form of restricted stock unit agreement	S-8	333-225294	99.1	5/30/2018	
10.6	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	
10.7+	Severance Agreement, dated August 1, 2016, by and between the Registrant and Dinesh Patel.	S-1/A	333-212476	10.9	8/1/2016	
10.8+	Severance Agreement, dated August 1, 2016, by and between the Registrant and David Y. Liu, Ph.D.	S-1/A	333-212476	10.10	8/1/2016	
10.9+	Employment Offer Letter, dated May 21, 2018, by and between the Registrant and Samuel Saks, M.D.	10-Q	001-37852	10.2	8/7/2018	
10.10†	Research and Collaboration Agreement, dated June 16, 2012, by and among the Registrant, Protagonist Pty. Ltd. and Zealand Pharma A/S.	S-1	333-212476	10.17	7/11/2016	
10.11†	Contract Extension Letter of Agreement, dated June 1, 2013, by and among the Registrant, Protagonist Pty. Ltd. and Zealand Pharma A/S.	S-1	333-212476	10.18	7/11/2016	
10.12†	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	333-212476	10.19	7/11/2016	
10.13†	Protagonist Assumption of Responsibility, dated January 28, 2014, by and between the Registrant and Zealand Pharma A/S.	S-1	333-212476	10.20	7/11/2016	
10.14†	Agreement to Assign Patent Applications, dated February 7, 2014, by and between the Registrant, Protagonist Pty. Ltd. and Zealand Pharma A/S.	S-1	333-212476	10.21	7/11/2016	

Exhibit Number	Exhibit Description	Incorporation By Reference				Filed Herewith
		Form	SEC File No.	Exhibit	Filing Date	
10.15†	Abandonment Agreement, dated February 28, 2014, by and among the Registrant, Protagonist Pty. Ltd. and Zealand Pharma A/S.	S-1	333-212476	10.22	7/11/2016	
10.16†	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	
10.17	Registration Rights Agreement, dated August 8, 2018, by and between the Registrant and certain parties identified on the signature pages thereto	8-K	001-37852	4.3	8/7/2018	
10.18	Securities Purchase Agreement, dated August 6, 2018, by and between the Registrant and certain purchasers identified on the signature pages thereto	S-3	333-227216	10.1	9/7/2018	
10.19	Exchange Agreement, dated December 21, 2018, by and between the Registrant and Biotechnology Value Fund, L.P., Biotechnology Value Fund II, L.P. and Biotechnology Value Trading Fund OS, L.P.	8-K	001-37852	10.1	12/31/2018	
10.20	First Amendment, dated January 31, 2019, to Lease, dated March 6, 2017, by and between Protagonist Therapeutics, Inc., as Tenant, and BMR-Pacific Research Center LP, as Landlord.	10-Q	001-37852	10.3	5/8/2019	
10.21+	Severance Agreement, dated March 14, 2019, by and among Protagonist Therapeutics, Inc. and Suneel Gupta, Ph.D.	10-Q	001-37852	10.4	5/8/2019	
10.22#	First Amendment to Exclusive License and Collaboration Agreement, by and between Protagonist Therapeutics, Inc. and Janssen Biotech, Inc., dated May 7, 2019.	10-Q	001-37852	10.1	8/7/2019	
10.23+	Offer Letter, by and between Protagonist Therapeutics Inc. and Donald Kalkofen, dated May 20, 2019.	8-K	001-37852	10.1	5/29/2019	
10.24+	Severance Agreement, dated July 19, 2019, by and between Protagonist Therapeutics, Inc. and Samuel Saks, M.D.	10-Q	001-37852	10.1	11/6/2019	
10.25	Credit and Security Agreement, dated October 30, 2019, by and between Protagonist Therapeutics, Inc., MidCap Financial, and Silicon Valley Bank.					X
10.26	Open Market Sale Agreement℠, dated November 27, 2019, by and between Protagonist Therapeutics, Inc. and Jefferies LLC.	8-K	001-37852	10.1	11/27/2019	
21.1	List of Subsidiaries					X

Exhibit Number	Exhibit Description	Incorporation By Reference				Filed Herewith
		Form	SEC File No.	Exhibit	Filing Date	
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
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.

Portions of this exhibit (indicated by hashtag) have been omitted as the registrant has determined that (i) the omitted information is not material and (ii) the omitted information would likely cause competitive harm to the registrant if publicly disclosed.

Item 16. Form 10-K Summary

None.

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 10, 2020

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 Don Kalkofen, 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 10, 2020
/s/ Don Kalkofen Don Kalkofen	Chief Financial Officer *(Principal Financial and Accounting Officer)*	March 10, 2020
/s/ Harold E. Selick, Ph.D. Harold E. Selick, Ph.D.	Chairman of the Board of Directors	March 10, 2020
/s/ Bryan Giraudo Bryan Giraudo	Director	March 10, 2020
/s/ Chaitan Khosla, Ph.D. Chaitan Khosla, Ph.D.	Director	March 10, 2020
/s/ Sarah Noonberg, M.D., Ph.D. Sarah Noonberg, M.D., Ph.D.	Director	March 10, 2020
/s/ William D. Waddill William D. Waddill	Director	March 10, 2020
/s/ Lewis T. Williams, M.D., Ph.D. Lewis T. Williams, M.D., Ph.D.	Director	March 10, 2020