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, 2016

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.)**
521 Cottonwood Drive, Suite 100 Milpitas, California 95035	
(Address, including zip code, of registrant's principal executive offices)	**(408) 649-7370 (Telephone number, including area code, of registrant's principal executive offices)**

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

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

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

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

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

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

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

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

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

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

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 registrant's common stock was not publicly traded as of the last business day of the registrant's most recently completed second fiscal quarter.

Number of shares of Common Stock outstanding as of February 28, 2017 was 16,787,990.

DOCUMENTS INCORPORATED BY REFERENCE:

Portions of the registrant's definitive Proxy Statement for the registrant's 2017 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, 2016.

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PART I

Statement made in this Annual Report on Form 10-K contains 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. 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 with a proprietary technology platform focused on discovering and developing peptide-based new chemical entities ("NCEs") to address significant unmet medical needs. Our primary focus is on developing first-in-class oral peptide drugs that specifically target the same biological pathways also targeted by currently marketed injectable antibody drugs. Compared to injectable antibody drugs, our oral peptides offer targeted delivery to the gastrointestinal ("GI") tissue compartment, potential for improved safety due to minimal exposure in the blood, improved convenience and compliance due to oral delivery and the opportunity for earlier introduction of targeted therapy for inflammatory bowel disease ("IBD"). Our initial lead product candidates, PTG-100 and PTG-200, are based on this approach and we believe they have the potential to transform the existing treatment paradigm for IBD, a GI disease consisting primarily of ulcerative colitis ("UC"), and Crohn's disease ("CD").

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

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

Our Product Candidates

PTG-100

PTG-100 has first-in-class potential as an oral, alpha-4-beta-7 (" α 4 β 7") integrin-specific antagonist for the treatment of IBD. The α 4 β 7 integrin is considered to be one of the most GI-specific biological targets for IBD. It is a cell surface protein present on T cells that plays an important role in the trafficking of T cells to the GI tissue compartment by binding to MAdCAM-1, an extracellular protein that resides mostly in the GI vasculature.

We are leveraging several factors to inform and guide the clinical development of PTG-100 for the treatment of IBD. First, PTG-100 shares the same α 4 β 7 integrin target as the injectable antibody drug vedolizumab, marketed as Entyvio ® , for the treatment of moderate-to-severe UC and CD. Second, we utilized pharmacodynamic ("PD") biomarker assays similar to those described in scientific publications used with Entyvio ® and other antibodies in development as indicators of target engagement to establish proof-of-concept ("POC") in our Phase 1 clinical trial with PTG-100. These PD data include increases in receptor occupancy and decreases in receptor expression. We believe that we can utilize published information describing the development and regulatory path of Entyvio ® and other approved antibody drugs for IBD to help inform the design of our clinical development studies.

We have completed extensive pre-clinical studies of PTG-100 in which we established pharmacological POC, including effects on T cell trafficking and mucosal healing similar to comparator α 4 β 7 rodent antibody, DATK-32. Following the submission and approval of a Clinical Trial Notification ("CTN") in Australia in December 2015, we initiated a Phase 1 clinical trial, comprised of three components: a single ascending dose ("SAD") and multiple ascending dose ("MAD") component, each of which evaluated safety, pharmacokinetics ("PK"), and PD-based POC in healthy subjects, using an oral liquid formulation of PTG-100. The Phase 1 clinical trial was completed in June 2016. Dose escalation proceeded up to 1,000 mg, the highest dose tested in the study for both single and multiple dosing. There were no serious adverse events reported in the Phase 1 clinical trial, and no dose-limiting toxicities were observed. All reported adverse events were of mild to moderate severity. There were no dose-dependent increases observed for any adverse events. The most frequent adverse events reported by subjects on PTG-100 were headache and upper respiratory tract infection. These events were also observed in subjects who took placebo.

We initiated a global Phase 2b randomized, double-blinded, placebo-controlled dose-finding clinical trial in the fourth quarter of 2016 to assess safety and efficacy of PTG-100 in moderate-to-severe UC patients. We anticipate that the trial will enroll approximately 240 subjects at approximately 100 sites in the United States, Canada, Europe (Western, Central, and Eastern), Asia, Australia, and New Zealand. The primary objectives of our Phase 2b clinical trial are to evaluate the safety and tolerability of PTG-100 and its efficacy in the induction of remission in subjects with moderate-to-severe UC. Secondary objectives are to select PTG-100 induction doses for continued development, to characterize PTG-100 plasma concentrations and pharmacodynamic responses, and to evaluate any immunogenicity over 12 weeks. The trial will include subjects who have had prior exposure to tumor necrosis factor-alpha ("TNF- α ") inhibitors and subjects who have not been treated with biologics. Subjects will be randomized to one of four dose arms (150mg/300mg/900mg PTG-100 or placebo) for 12 weeks of once-daily oral dosing, followed by four weeks of safety follow-up. An interim futility analysis is expected to be performed in the second half of 2017, and if futility criteria are not met, one or two PTG-100 doses will be selected for continued randomization of the remaining subjects. We expect to complete the study and report top-line data in the second half of 2018. We expect that this trial will support end-of-Phase 2 meetings with global health authorities and enable the initiation of a Phase 3 pivotal program.

The primary endpoints are consistent with those used in the clinical development of previously approved drugs for UC. The trial is statistically powered to detect a clinically meaningful difference in induction of remission in subjects with moderate-to-severe UC who are treated with PTG-100 compared to placebo. The evaluation of clinical remission is based on the Mayo Score, which is a well-established composite assessment that utilizes patient-reported outcomes and endoscopic improvement. Secondary efficacy endpoints will include

endoscopic response, clinical response, endoscopic remission, change in endoscopic subscore, change in stool frequency and rectal bleeding subscores, change in fecal calprotectin, change in the IBD questionnaire, change in Mayo score and change in partial Mayo score, from baseline to multiple points during the induction period.

We plan to develop PTG-100 initially for the treatment of moderate-to-severe UC, potentially followed by mild-to-moderate UC, CD, and pediatric IBD, the latter being an orphan indication.

PTG-200

Our second oral, GI-restricted peptide product candidate is PTG-200, a potential first-in-class Interleukin-23 receptor ("IL-23R") specific antagonist for the treatment of IBD. Interleukin-23 ("IL-23") is a member of the IL-12 family of pro-inflammatory cytokines, and is a protein that regulates inflammatory and immune function and plays a key role in the development of IBD. By blocking the IL-23 receptor with PTG-200 in the GI tissue compartment, we expect to reduce inflammation while potentially minimizing the risk of systemic side effects due to its GI-restricted nature. The IL-23 pathway is targeted by the IL-12 and IL-23 antagonist infused antibody drug ustekinumab, marketed as Stelara ® , for psoriasis, psoriatic arthritis, and moderate-to-severe CD.

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

PTG-300

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

Additional Product Candidates. We are currently researching potential oral and injectable peptide-based product candidates for a range of conditions including, but not restricted to GI diseases.

The Evolution of Antibody Drugs for Targeted Therapy and Their Limitations

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

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

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

- *Injections or infusions are associated with significant patient burden.* Antibody drugs are large proteins that are not stable in the GI tissue compartment. As a consequence, antibody based therapies are administered primarily by injection or infusion into systemic circulation. Injections or infusions as a mode of delivery can increase patient burden, including site reactions and systemic hypersensitivity, inconvenience, and needle anxiety and phobia, each of which may negatively affect patient compliance.

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

Our Solution for IBD: Oral, GI-Restricted Peptides

Our novel peptide therapeutics platform may provide important benefits over existing non-targeted small molecule, injectable antibody, and conventional peptide therapeutics. In addition, our platform represents a major step forward in the evolution of peptides as therapeutics. Most of the more than 60 currently FDA approved peptides have unstructured shapes, leading to chemical and biological stability limitations, which confine their use to injectable drugs. In contrast, our peptide technology platform allows us to identify constrained peptides that can serve as a starting point for discovery and development of oral, selective, and potent peptides. The well-folded conformation in our constrained peptides is typically derived by disulfide bonds, a structural feature inherent in many naturally occurring peptides. For the IBD targets of interest, the size and nature of our peptides is carefully selected and modified so as to acquire the desired potency and specificity, and also to restrict their presence to the GI tissue compartment when administered orally. These features translate to oral, GI-restricted, selective and potent peptide drug candidates with specific advantages compared to antibody drugs:

- *Oral administration* . We are developing our peptide therapeutics in a convenient capsule or tablet form intended for oral administration. We believe oral administration may reduce many of the problems and limitations associated with injections or infusions, including injection site pain and local reactions, inconvenience, anxiety, high rates of immunogenicity and potential safety risks.
- *Potential for improved safety and tolerability compared to antibody drugs.*
  - *Oral and GI-restricted delivery minimizes systemic exposure in the blood.* Oral GI-restricted delivery results in lower drug levels in the blood that may provide the potential for an enhanced safety profile over antibody drugs.
  - *Peptides can be cleared more quickly from systemic circulation.* Small molecules and peptides below a size threshold can be rapidly cleared from blood circulation by kidney filtration and excretion. Rapid clearance may be beneficial especially if patients need to discontinue therapy. In contrast, antibody drugs, because of their long plasma half-life, may take months to clear from blood circulation leaving patients exposed to continued or increased safety risk.

- *The likelihood of much lower immunogenicity of small stable peptides compared to antibody drugs reduces the risk of loss of response.* We believe that ADAs are less likely to be elicited against constrained peptides, due to their small size, lack of epitope density, resistance to proteolysis, oral tolerance, and minimal systemic absorption.

- *Potential for localized delivery to site of disease.* We believe oral dosing of GI-restricted peptides results in substantially higher drug concentrations in the diseased GI tissue compartment compared to injectable antibody drugs. This targeted delivery to the site of action may lead to more immediate and significant target engagement at the site of active disease in the GI tissue compartment.

- *Cost-effective and less complex manufacturing* . Because of their size and stability, we believe that our oral, GI-restricted peptide product candidates can be produced, stored and shipped in a more cost-effective manner than many antibody drugs.

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

Overview of Inflammatory Bowel Disease

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

Market Overview

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

History of IBD Treatments

Non-Targeted Therapies

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

TNF- α and α 4 β 7 Integrin Targeted Antibody Drugs

Recent advances in molecular biology and genomics ushered in the development of the potent and highly targeted biologic drugs. TNF- α was identified as a cytokine, a protein involved in cell signaling, that plays an important role in the inflammatory processes associated with IBD. In developing therapies against TNF- α , small molecule antagonists that directly bind TNF- α and other PPI targets have yet to be discovered and approved as therapeutics for the treatment of IBD. Thus, monoclonal antibody drugs emerged as a new class of therapeutics that can inhibit TNF- α activiy. There are currently five TNF- α antibody drugs (Humira ® , Remicade ® , Cimzia ® , Simponi ® and Inflectra ® (infliximab biosimilar)) approved for the treatment of UC and/or CD. In 2014, Entyvio ® , an intravenously administered antibody that selectively targets the α 4 β 7 integrin, was approved for the treatment of adult patients with moderate-to-severe UC or CD where one or more standard therapies have not resulted in an adequate response. Entyvio ® sales were approximately $530 million in 2015 and are projected to peak at approximately $2 billion.

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

The Evolving IBD Treatment Paradigm

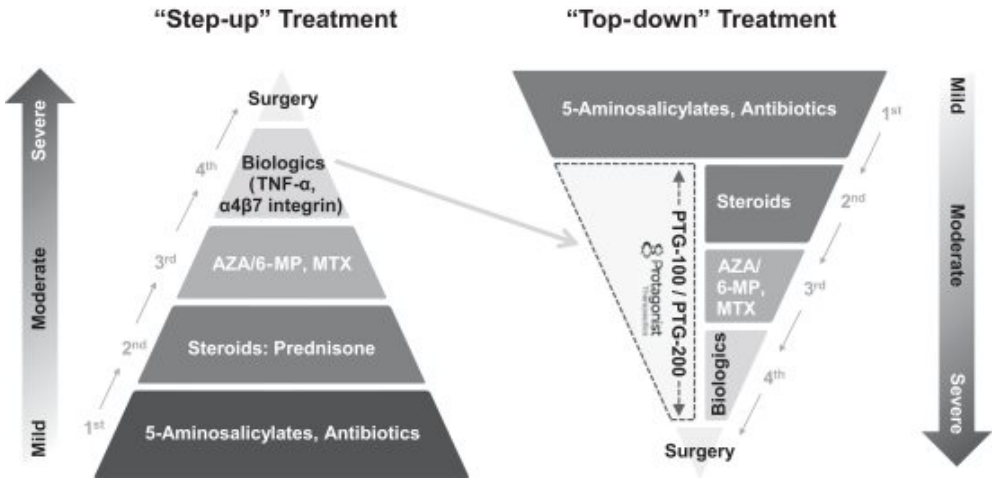
Inducing and maintaining clinical remission is the primary goal of treatment for IBD patients. The current treatment paradigm for IBD is considered a “step-up” approach. It involves a sequential “step-up” in treatment to more potent but higher risk therapies according to the level of severity of the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

For moderate-to-severe IBD patients, physicians may prescribe TNF - α antibody drugs (e.g. Remicade ® or Humira ®) or Entyvio ® , an antibody drug inhibiting α 4 β 7 integrin, to induce and maintain clinical remission. Patients who are transitioned to these targeted antibody drugs may fail to respond to treatment or lose response to some or all of these agents over time and may ultimately require surgery. Approximately 50% to 73% of CD and 65% of UC patients fail to reach remission with TNF- α antibodies. Furthermore, 30% to 40% of UC patients and approximately 40% of CD patients treated with TNF- α antibody drugs stop responding to these agents over time (secondary non-responders) at a rate of approximately 10% to 13% per year. Of the CD patients who initially benefit from TNF- α antibody drugs, 25% to 40% of these patients develop intolerable or serious adverse events or lose their response within the first year of therapy. Currently, a common approach for IBD patients with lack of efficacy or loss of response to TNF- α antibody drugs is to switch such patients to other TNF- α antibody drugs. Although this is initially successful in 40% to 60% of patients, there remains a lack of treatment options for patients who lose responses to multiple TNF - α antibody drugs. Further, patient non-adherence with TNF- α antibody drugs in IBD has been reported to be between approximately 30% to 45% resulting in a greater need for hospitalization.

The development of new, potent and targeted therapies for IBD with oral delivery may potentially offer more effective treatment options for moderate-to-severe IBD patients. Furthermore, many clinicians are already advocating for an earlier introduction of targeted therapeutics in IBD to reduce, replace or delay the use of corticosteroids and non-specific oral immunomodulators. This treatment approach is often referred to as a “top-down” approach as therapeutics that are currently at the top of the “step-up” pyramid are moved down to earlier in the treatment paradigm (see Figure 1). We believe we are well-positioned to be leaders in this shift from “step-up” to “top-down” therapy. Our oral, GI-restricted, and targeted peptide drugs work on the same specific targets as injectable antibody drugs and have the potential to offer improved patient safety, improved compliance and convenience and reduced immunogenicity as compared to antibody drugs. In addition, key opinion leaders are increasingly viewing the α 4 β 7 integrin antagonist Entyvio ® as a preferable alternative to TNF- α blockers for the

treatment of IBD due to its improved safety profile. Taken together, we believe that these trends may result in our product candidates, if approved, being used more broadly than antibody drugs in moderate-to-severe IBD patients and potentially being used for the treatment of mild-to-moderate disease.

Figure 1: Transforming the Existing IBD Treatment Paradigm with Oral Targeted Therapy Drugs



PTG-100: AN ORAL α 4 β 7 INTEGRIN ANTAGONIST

PTG-100 was discovered through our peptide technology platform and is being developed as a potential first-in-class oral, GI-restricted α 4 β 7 integrin-specific antagonist initially for patients with moderate-to-severe UC.

Mechanism of Action

Integrins, such as α 4 β 7, are transmembrane proteins that regulate cellular movement into extravascular tissue and play an important role in modulating the inflammatory reaction in the gut. The α 4 β 7 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 α 4 β 7 T cells into the GI tissue compartment and their subsequent activation within the GI tissue compartment. The entry of α 4 β 7 T cells into the GI tissue compartment is facilitated by the PPI between the α 4 β 7 integrin and its corresponding ligand, MAdCAM-1, which is primarily expressed in the GI tissue compartment. Hence, the binding of α 4 β 7 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 α 4 β 7 integrin to MAdCAM-1, PTG-100 may prevent T cells from entering the GI tissue compartment, thereby reducing inflammation that leads to the clinical manifestations of UC.

α 4 β 7 for IBD is targeted by FDA-approved Entyvio ® (vedolizumab), which has demonstrated safety and efficacy in patients with moderate-to-severe UC and CD. Since PTG-100 targets the same biological pathway as Entyvio ® , we can utilize similar PD-based POC as early as in our pre-clinical studies and Phase 1 clinical trial to inform and guide our Phase 2b development program. We sourced these PD biomarker assays from public scientific publications and do not maintain any contractual arrangement providing access to this information with the makers of these marketed products.

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

We have established a potentially efficacious dose range of PTG-100 in mice by demonstrating similar pharmacologic activity between oral PTG-100 and an injectable α 4 β 7 antibody in mouse models of IBD. From this

efficacious dose range in mice, approximately 6-50 mg/kg per day, we are able to directly estimate a potentially efficacious dose range in humans through allometric scaling based on whole body surface areas, which we determined to be approximately 33-300 mg per day.

Concurrently, we employed a complementary approach for establishing a potentially efficacious human dose range and early POC through specific blood PD response markers that reflect α 4 β 7 integrin target engagement of PTG-100 in the GI tissue compartment and correlated those PD measurements with efficacy responses in mouse colitis models. Target engagement is a critical feature for demonstrating that PTG-100 can reach its intended target, thus inhibiting the trafficking of T cells into the GI tissue compartment. Our PD markers were monitored in mice and cynomolgus monkeys ("cyno"), which were similarly evaluated in normal healthy volunteers in our Phase 1 clinical trial. These blood PD responses demonstrated that PTG-100 engaged its intended α 4 β 7 target and helped guide human dosing for our Phase 2b clinical trial.

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

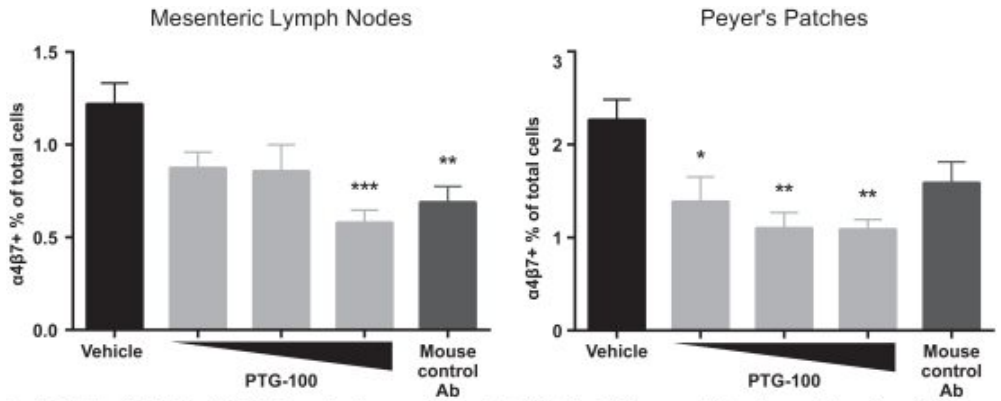
Pre-clinical studies have demonstrated that PTG-100 is a potent and highly selective α 4 β 7 antagonist with minimal systemic absorption. Mouse colitis models have further demonstrated that PTG-100 can inhibit T cell trafficking in the gut similar to the actions of the mouse α 4 β 7 antagonist antibody.

PTG-100 potently inhibited binding of α 4 β 7 to MAdCAM-1 in several human biochemical enzyme-linked immunosorbent assay ("ELISA") and cell adhesion (transformed and primary cells) assays in a low nanomolar concentration range sufficient to inhibit 50% of binding ("IC50") comparable to vedolizumab. PTG-100 exhibited greater than a 100,000-fold selectivity against other structurally similar integrins, α 4 β *1* and α L β 2, in cell adhesion assays which is comparable to the selectivity of vedolizumab. PTG-100 was stable in *in vitro* assays simulating the GI tissue compartment, such as the small intestine and gastric stomach, with half-lives exceeding 12 hours and in human liver microsomes suggesting strong oral stability and the potential for once daily dosing in humans. PTG-100 did not affect the growth of and was not metabolized by common members of the human intestinal microflora. In total, these drug properties provide evidence to characterize PTG-100 as a potential first-in-class orally stable α 4 β 7-specific antagonist. Furthermore, these drug properties allowed us to demonstrate proof-of-concept in animal colitis studies.

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

We designed mouse colitis studies similar to those used for antibody drugs targeting this pathway to specifically monitor T cell trafficking to and from the GI tissue compartment (Figure 2). PTG-100 reduced α 4 β 7 memory T cells migrating to the gut lymphoid tissues, including the mesenteric lymph nodes ("MLN") and Peyer's patches ("PP"), under inflammatory conditions in the GI tissue compartment. Another example of the ability of PTG-100 to inhibit T cell trafficking was demonstrated by the reduction in the number of α 4 β 7 cells in colon lesions in colitis mice. Furthermore, treatment benefit was demonstrated through blinded video endoscopy analysis for mucosal damage, and assessment of the incidence of bloody feces, which represent symptoms and measurements of UC in humans. In all studies in mouse models of colitis, the effects of oral PTG-100 were comparable to those of an injection of high doses of a positive control α 4 β 7 antibody. This allows us to define the efficacious dose in mice with potential translation to the efficacious dose in humans.

Figure 2: PTG-100 Reduces Trafficking of Memory T Cells to MLN and Peyer's Patches

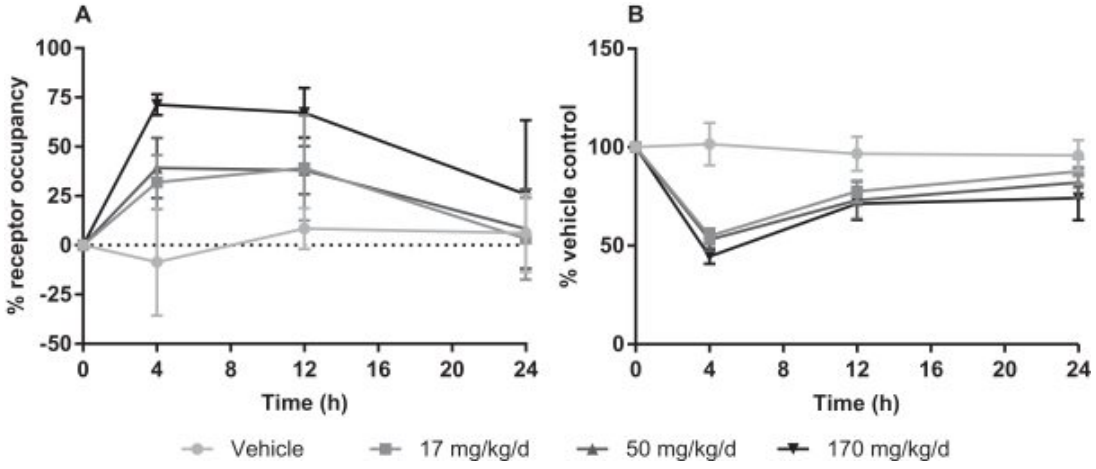


*** p≤0.05; ** p≤0.01; *** p≤0.001. A p-value is a measure of statistical significance of the observed result, or the probability that the observed result was achieved purely by chance. By convention, a p-value of 0.05 or lower is considered statistically significant (a p-value of <0.05 means that there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

Establishing Blood Pharmacodynamic Readouts of Target Engagement

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

Figure 3: (A) Percent Receptor Occupancy and (B) Receptor Expression of α 4 β 7 on CD4+ Memory T Cells in Blood of Healthy Mice Dosed for 14 Days



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

To date, all toxicology and safety pharmacology studies have not identified any safety issues. Good Laboratory Practices ("GLP") toxicology studies in rats and cyno over 42 days and 12 weeks of dosing showed that PTG-100 was well-tolerated at all dose levels with no dose-limiting toxicities. GLP are those procedural and operational requirements specified by FDA regulation to ensure the validity and reliability of nonclinical studies. No adverse effects were seen in either rat or cyno studies at all doses tested. Standard safety pharmacology and genotoxicity studies were similarly negative. We are currently conducting chronic GLP toxicology studies to support our anticipated Phase 3 program.

PTG-100's Phase 1 Clinical Trial Overview

Following the submission and approval of a CTN, we initiated a Phase 1 randomized, double-blind, placebo-controlled clinical trial of PTG-100 in 78 normal healthy male volunteers in Australia, which was completed in June 2016. The Phase 1 SAD and MAD components were conducted with a solution-based liquid formulation of PTG-100. In the formulation bridging component of the trial, we compared the relative bioavailability of the liquid formulation to the capsule formulation that is being used in Phase 2b. In addition to determining the safety and tolerability and PK of PTG-100, the SAD and MAD components of the trial evaluated PD-based POC through the assessment of α 4 β 7 receptor occupancy that indicates target engagement and α 4 β 7 target expression on peripheral blood memory T cells similar to what was done in the pre-clinical studies.

Safety and Tolerability

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

Pharmacokinetics

PTG-100 plasma levels increased in a dose-dependent manner in both single and multiple dosing cohorts. Consistent with the pre-clinical data in mice, rats, and cyno, the blood levels of PTG-100 were extremely low as

determined by the Area Under the Curve (AUC, which is a pharmacokinetic measurement of drug exposure in blood plasma against time) and Cmax (maximum concentration), thus demonstrating the GI-restricted nature of the drug. There was no apparent evidence of drug accumulation at Day 14 in the MAD cohorts perhaps related to the relatively short half-life ("T1/2") in the blood.

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

Establishing Pharmacodynamic POC in Humans

Data from our mouse colitis studies support our conclusion that blood receptor occupancy is a correlate of target engagement in the GI tissue compartment in the dose ranges studied. In our Phase 1 clinical trial, blood receptor occupancy on CD4+ memory α 4 β 7+T cells increased in a dose-dependent and time-dependent manner. For receptor occupancy in the SAD cohorts, treatment groups were significant compared to placebo at 100 mg ($p \leq 0.05$), 300 mg ($p \leq 0.005$) and 1,000 mg ($p \leq 0.0001$). In the MAD cohorts, treatment groups were significant compared to placebo at 100 mg ($p<0.0005$), 300 mg ($p<0.0001$) and 1,000 mg ($p<0.0001$) four hours post dose on Day 14.

An additional parameter of pharmacologic activity that we measured was the change in α 4 β 7 expression on the blood memory T cells. Based on *in vitro* studies comparing vedolizumab and PTG-100, we expected that α 4 β 7 expression would be reduced over time due to the internalization of the α 4 β 7 receptor. Following single and multiple dose administration in the Phase 1 clinical trial, a dose-dependent and time-dependent reduction in α 4 β 7 expression was observed, and it appears that the reduction in target expression may become saturated at 300 mg since a similar response was observed in the 1,000 mg cohort following both single and multiple dosing. For α 4 β 7, downregulation of expression was significant in treatment groups, compared to placebo at 300 mg and 1,000 mg ($p \leq 0.01$).

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

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

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

We utilized a liquid formulation in the SAD and MAD components of the Phase 1 clinical trial. To support the use of a capsule formulation in the Phase 2b study, we compared the PK in a single dose cross-over evaluation of the liquid and capsule formulation in normal healthy volunteers and observed that the plasma exposure of the capsule formulation was lower than that of the liquid formulation at the same dose level. The PD effects were highly similar between the capsule and liquid formulations, despite the lower plasma exposure of the capsule formulation.

PTG-200: AN ORAL IL-23R ANTAGONIST

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

Mechanism of Action and Rationale

IL-23 is a member of the IL-12 family of cytokines with pro-inflammatory and autoimmune properties. Cytokines are cell signaling proteins that are released by cells and affect the behavior of other cells. Binding of the IL-23 ligand to the IL-23R receptor leads to an expression of pro-inflammatory cytokines involved in the mucosal autocrine cascade that is an important pathway of many inflammatory diseases, including IBD. Furthermore, genetic analyses of IBD patients have implicated IL-23R mutations as a risk factor associated with susceptibility to IBD. The antagonist infused antibody drug ustekinumab (marketed as Stelara ® for psoriasis, psoriatic arthritis, and moderate-to-severe CD) is a p40 antagonist antibody that inhibits both the IL-23 and IL-12 pathways. Next-generation IBD antibody drugs, such as guselkumab, target the p19 subunit of the IL-23 ligand and are specific to the IL-23 pathway, which is believed to be an important driver of IBD pathology, while not blockading the IL-12 pathway. IL-12 is believed to be important in immune surveillance against the development of infections and malignancies.

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

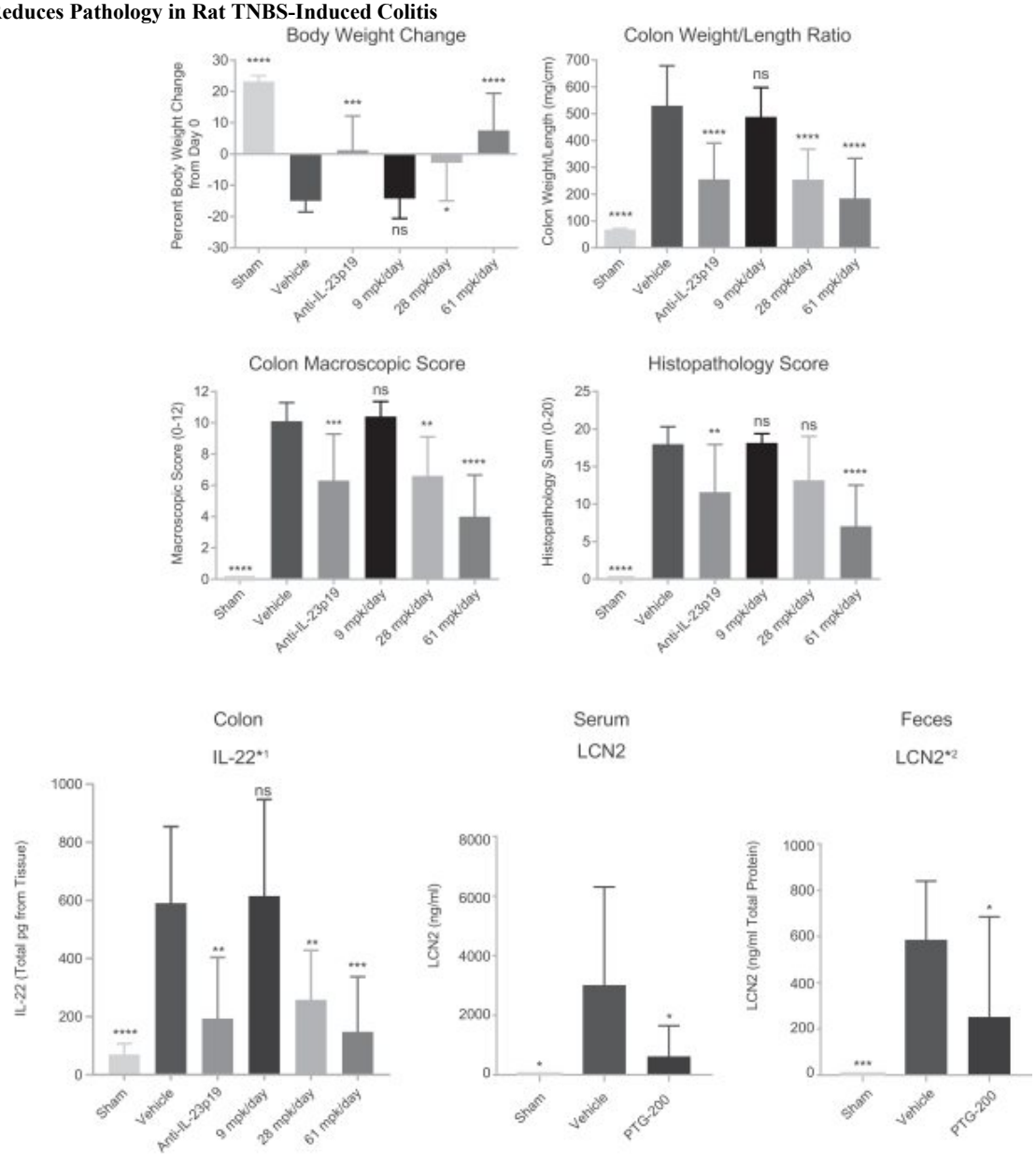
PTG-200's Pre-Clinical Proof-of-Concept Studies

PTG-200 potently inhibited binding of IL-23 to the IL-23 receptor in several biochemical (ELISA) and cell (transformed and primary) signaling assays in a subnanomolar to low nanomolar concentration range sufficient to inhibit 50% of binding. PTG-200 exhibited greater than a 50,000-fold selectivity against other structurally similar receptors (IL-12R β 1 and IL-6R) thereby potentially reducing the risk of off target interactions. In total, these drug properties provide evidence to characterize PTG-200 as a potential first-in-class orally stable IL-23R-specific antagonist.

In PK studies in rats and cyno, PTG-200 was GI-restricted with less than 0.5% oral systemic bioavailability in plasma or urine and principal exposure in the small intestine, colon, and feces. Similar results were observed in cyno.

We have also completed pre-clinical POC studies in rat 2, 4, 6-trinitrobenzenesulfonic acid (TNBS) colitis models demonstrating that oral delivery of PTG-200 and other prototype antagonists significantly improved disease outcomes, such as reducing body weight loss, reducing the increased colon weight/length ratio, and reducing the increased colon macroscopic score which is comprised of assessments of colon adhesions, strictures, ulcers, and wall thickness in a dose dependent manner (Figure 4). Furthermore, PTG-200 was found to reduce the increased histopathology summary score, which is comprised of assessments of mucosal and transmural inflammation, gland loss, and erosion parameters. Finally, PTG-200 was able to reduce the expression of the pro-inflammatory IL-23 induced cytokines in the colon and the IBD disease biomarker lipocalin (LCN2) in the serum and feces (Figure 4).

Figure 4: PTG-200 Reduces Pathology in Rat TNBS-Induced Colitis



*1 Similar effects observed with IL-17A and MPO

*2 Similar effects observed with MPO

Statistical significance was assessed by One-way ANOVA with post-hoc Dunnett's method versus Vehicle control: *p≤0.05; **p≤0.01; ***p≤0.001; ****p≤0.0001; ns, not significant.

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

PTG-200's Preliminary Pre-Clinical Safety Studies

In preliminary non-GLP toxicity studies in rats, PTG-200 was well-tolerated with no adverse events at the highest dose level tested. We have initiated 3 month GLP toxicology, safety pharmacology, genotoxicity, and current good manufacturing practice ("cGMP") manufacturing studies in support of starting a Phase 1 clinical trial in 2017.

Proposed Clinical Plans

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

PTG-300: AN INJECTABLE HEPCIDIN MIMETIC

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

Mechanism of Action

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

Overview of β -Thalassemia and Current Therapies

β -Thalassemia is potentially our first clinical indication for PTG-300. Due to repeat transfusions and/ or increased absorption of iron, patients with β -Thalassemia frequently suffer from iron overload which can lead to significant morbidity and mortality. This iron overload is exacerbated in those β -Thalassemia patients who require chronic blood transfusions for survival. A hepcidin mimetic such as PTG-300 will potentially be able to correct the anemia caused by the genetic mutation underlying β -Thalassemia, thus giving it a dual benefit of increasing the production of red blood cells, reducing excess circulating iron, and reducing splenomegaly.

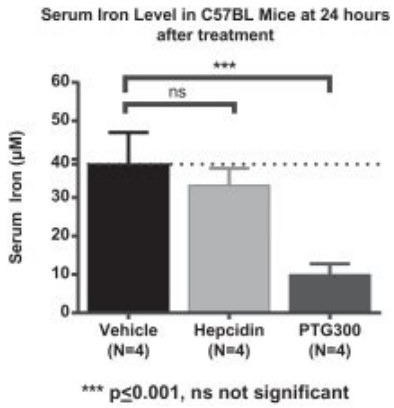
Globally, prevalence of β -Thalassemia is estimated to be approximately 200,000, with at least 60,000 patients born each year with the disease. In 2010, the β -Thalassemia market was estimated to be greater than $500 million, based largely on drugs consisting of chelating agents used to treat iron overload disorders. The

market is expected to grow to nearly $1 billion by 2018. β -Thalassemia has low prevalence in the Americas, with an estimated 2,750 patients and with approximately 300 patients born each year with the disease. Therefore, β -Thalassemia may qualify for FDA orphan designation.

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

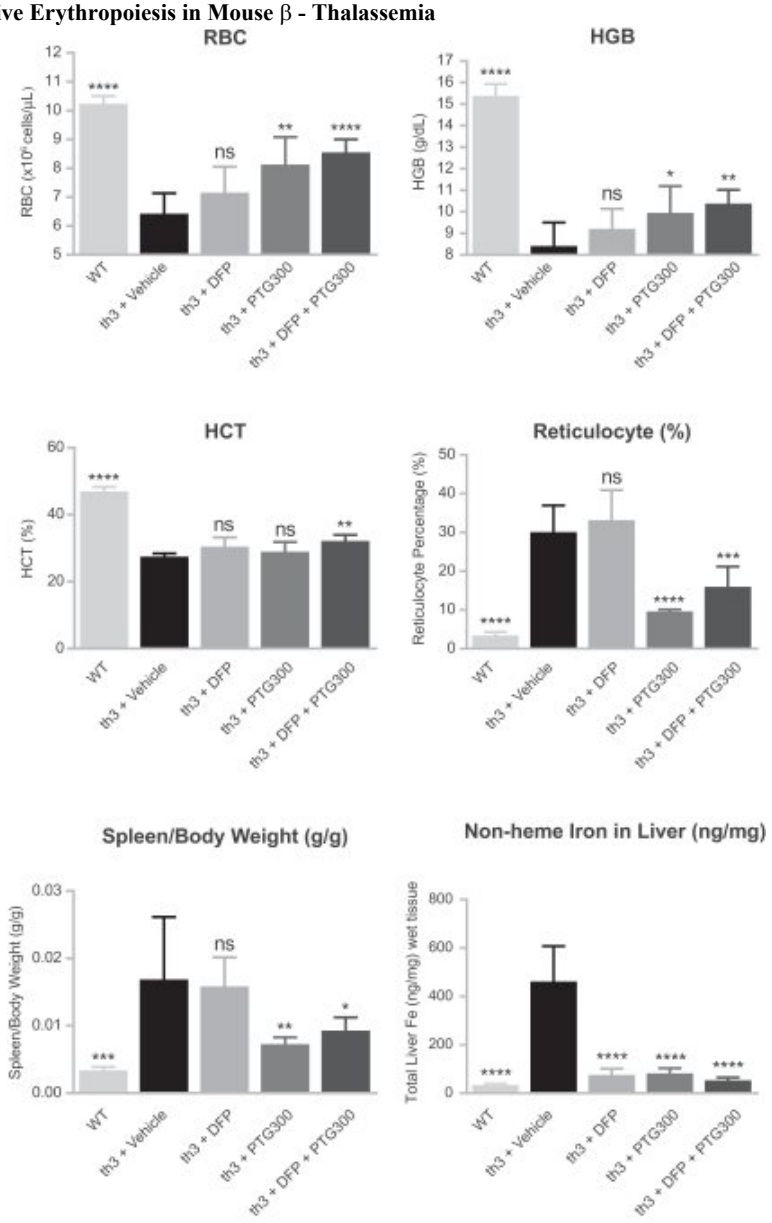
In pre-clinical studies, we demonstrated that PTG-300 can lower serum iron more effectively than hepcidin and maintain such lowered serum iron levels for at least 24 hours following a single subcutaneous injection (Figure 5). We have also demonstrated that PTG-300 in a dose dependent manner can reduce serum iron in healthy mice, rats, and cyno.

Figure 5: PTG-300 is More Effective Than Hepcidin in Lowering Serum Iron in Healthy Mice



PTG-300 was also able to address the underlying anemia present in a mouse genetic model of b-Thalassemia, as shown most prominently by the significant increase in red blood cell number (RBC) and hemoglobin (HGB) with the corresponding decrease in reticulocyte content (Figure 6). As a consequence we also observed a significant reduction in the pathological increases in spleen weight (splenomegaly) by addressing the underlying ineffective erythropoiesis. Furthermore, PTG-300 was effective in reducing the increase in liver iron content. In contrast the oral iron chelator deferiprone (DFP) did not correct the anemia or the splenomegaly.

Figure 6: PTG-300 Addresses Ineffective Erythropoiesis in Mouse β - Thalassemia



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

PTG-300's Development Program

PTG-300 is being manufactured and formulated to support completion of pre-clinical GLP toxicology, genotoxicity, and safety pharmacology studies, which will enable us to complete a single ascending dose Phase 1 clinical trial in normal healthy volunteers in 2017. This study will evaluate safety/ tolerability, PK and PD-based POC through the evaluation of PTG-300's effect on serum iron levels.

OUR PEPTIDE TECHNOLOGY PLATFORM

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

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

The key foundations of the platform include:

Molecular design tools and large database of constrained scaffolds

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

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

Phage display techniques and cluster libraries

Phage display may be used to discover the original hit based on Vectrix ™ -derived scaffolds, optimize existing hits, or to identify hits against those targets in which no structural information exists. For the latter

targets, a series of pre-existing phage libraries, termed cluster libraries, are used for hit discovery. This includes 20 proprietary libraries of structurally diverse DRPs that sample greater than 85% of their known structural diversity and 14 proprietary libraries that sample different protein loop geometries. Collectively these libraries provide immense potential for discovering hits at diverse targets as they are based on natural-DRP scaffolds with these characteristics.

Oral stability and in vitro and ex vivo assays

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

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

Medicinal peptide chemistry

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

In vivo pharmacology tools for GI restriction

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

Future Applications of our Platform

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

Material Agreements

Research Collaboration and License Agreement with Zealand Pharma A/S

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

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

Letter Agreement with Johnson & Johnson Development Corporation

In May 2013, in connection with our sale of Series B Stock, we entered into a letter agreement with Johnson & Johnson Development Corporation ("JJDC"), as amended on April 19, 2016, pursuant to which we granted JJDC a right of first negotiation with respect to the consummation of any proposed sale, transfer, license, commercialization or distribution arrangement (each, a "Transaction") of our inventions, developments, patents, patent applications, know-how or other proprietary rights or products controlled by us that are necessary for the research, development or commercialization of the PTG-100, PTG-200 and IL-13 programs (each, a "Program") other than an acquisition, merger, consolidation, or sale of substantially all of our assets. The letter agreement does not apply with respect to the PTG-300 program. The term of JJDC's right of first negotiation commenced in May 2014 and terminates, with respect to any Program, 60 days after our filing of an IND (or the foreign equivalent), with respect to each Program (such right of first negotiation period, the "ROFN Period"). On November 1, 2015, JJDC waived their right of first negotiation with respect to PTG-100. Neither we, nor JJDC, have an obligation to enter into a Transaction during the ROFN Period. We are not currently pursuing an IL-13 Program.

In the event that we receive a bona fide term sheet for a Program, we are obligated to notify JJDC of such offer (but not the terms thereof) and JJDC has a period of 30 days to notify us of exercise of its right to negotiate for a Transaction with JJDC. Following expiration of the ROFN Period with respect to any remaining Program, we are required to deliver to JJDC certain information relating to such Program, including pre-clinical results, manufacturing protocols and other information relevant to the evaluation of such Program, as determined by us. For a period of 60 days following delivery of such information (the "Exclusive Negotiation Period"), we are required to negotiate in good faith and exclusively with JJDC to enter into a Transaction with JJDC with respect to such Program and we are not permitted to enter into negotiations with any third party with respect to a Transaction involving such Program that would impair the ability of JJDC to exercise its rights under the letter agreement.

Finally, for a period of 180 days following expiration of an Exclusive Negotiation Period for a Program (the "Tail Period"), we are not permitted to enter into a Transaction with respect to such Program with a third party on terms that contain upfront payments and pre-launch milestones (valued on a risk-adjusted basis) that are inferior in total economic value to those that JJDC and its affiliates last offered to us, to the extent any such offer was previously made by JJDC or its affiliates to us.

JJDC's right of first negotiation with respect to any Program that has not earlier expired or been waived by JJDC will terminate upon the sale, transfer or other disposition by us of all or substantially all of our assets, our consummation of a merger or consolidation with or into another entity, or the transfer (whether by merger, consolidation, equity financing, or otherwise), in one transaction or a series of related transactions, to a person or group of affiliated persons a majority or more of our outstanding voting stock (or the surviving or acquiring entity).

Competition

The biotechnology and pharmaceutical industries are intensely competitive and subject to rapid and significant technological change. While we believe that our product candidates, technology, knowledge and experience provide us with competitive advantages, we face competition from established and emerging pharmaceutical and biotechnology companies, academic institutions, governmental agencies and public and private research institutions, among others. There are no approved oral peptide-based α 4 β 7 integrins and IL-23 based product candidates for IBD.

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

- Infused α 4ß7 antibody: Takeda Pharmaceutical Company
- Infused IL-23 and IL-12 antibody: Johnson & Johnson
- Injectable or infused TNF- α antibody: AbbVie, Johnson & Johnson, Amgen, Pfizer, UCB S.A.

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

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

Intellectual Property

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

Our commercial success may depend in part on our ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to our business; defend and enforce our patents; preserve the confidentiality of our trade secrets; and operate without infringing the valid enforceable patents and proprietary rights of third parties. Our ability to stop third parties from making,

using, selling, offering to sell or importing our products may depend on the extent to which we have rights under valid and enforceable patents or trade secrets that cover these activities. We cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our existing patents or any patents that may be granted to us in the future will be commercially useful in protecting our commercial products and methods of manufacturing the same. For more information, please see "Item 1A Risk Factors—Risks Related to Our Intellectual Property."

We have two issued patents and numerous patent applications related to our lead product candidates, and possess substantial know-how and trade secrets relating to the development and commercialization of peptide based therapeutic products. Our proprietary intellectual property, including patent and non-patent intellectual property, is generally directed to, for example, peptide-based therapeutic compositions, methods of using these peptide-based therapeutic compositions to treat or prevent disease, methods of manufacturing peptide-based therapeutic compositions, and other proprietary technologies and processes related to our lead product development candidates. As of February 10, 2017, our patent portfolio includes the following:

- two issued patents and approximately 44 patent applications that we exclusively own related to α 4 β 7 integrin peptide antagonists;
- approximately 13 patent applications that we exclusively own related to IL-23R antagonist peptides;
- approximately 24 patent applications that we exclusively own related to hepcidin analogues; and
- other patent applications that we license or exclusively own related to our core technologies, including methods of peptide modification and characterization.

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

α 4 β 7 Integrin Antagonist Peptides

The α 4 β 7 integrin antagonist peptide patent portfolio includes one issued U.S. patent and pending patent applications directed to compositions of α *4* β 7 integrin peptide monomers and dimers cyclized through intramolecular bonds and containing amino acid modifications conferring increased stability, potency and/or selectivity, as well as methods of synthesizing and using these antagonist peptides to treat inflammatory disorders. Applications are currently pending in the United States and other major jurisdictions, including Australia, Canada, China, Japan, and Europe. Patent applications directed to PTG-100 composition of matter and uses thereof, if issued from the pending patent applications and if the appropriate maintenance, renewal, annuity or other governmental fees are paid, are expected to expire in October 2035 (worldwide, excluding possible patent term extensions). We expect other patent applications in this portfolio, if issued, and if the appropriate maintenance, renewal, annuity, or other governmental fees are paid, to result in patents that would expire from October 2033 to March 2037 (worldwide, excluding possible patent term extensions).

IL-23R Antagonist Peptides

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

Hepcidin Mimetics Analogues

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

Other

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

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

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

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

Trade Secrets

We rely on trade secrets to protect certain aspects of our technology, particularly in relation to our technology platform. However, trade secrets can be difficult to protect. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our employees, consultants, scientific advisors and contractors. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our

consultants, contractors or collaborators use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions. For more information, please see "Item 1A Risk Factors—Risks Related to Our Intellectual Property."

Manufacturing

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

Government Regulation

The FDA and comparable regulatory authorities in state and local jurisdictions and in other countries impose substantial and burdensome requirements upon companies involved in the clinical development, manufacture, marketing and distribution of drugs, such as those we are developing. These agencies and other federal, state and local entities regulate, among other things, the research and development, testing, manufacture, quality control, safety, effectiveness, labeling, storage, record keeping, approval, advertising and promotion, distribution, post-approval monitoring and reporting, sampling and export and import of our product candidates.

U.S. Government Regulation

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

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

- completion of pre-clinical laboratory tests, animal studies and formulation studies in compliance with the FDA's GLP regulations;
- submission to the FDA of an IND application, which must become effective before human clinical trials may begin;

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

Pre-clinical Studies

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

Clinical Trials

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

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

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

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

Marketing Approval

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

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

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

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

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

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

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

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

Orphan Designation

The FDA may grant orphan designation to drugs or biologics intended to treat a rare disease or condition that affects fewer than 200,000 individuals in the United States, or if it affects more than 200,000 individuals in the United States, there is no reasonable expectation that the cost of developing and marketing the product for this type of disease or condition will be recovered from sales in the United States. Orphan designation must be requested before submitting a NDA or Biologics License Application ("BLA"). After the FDA grants orphan designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

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

Post-Approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling

claims are subject to prior FDA review and approval. There also are continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

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

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

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

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

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

Coverage and Reimbursement

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

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

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

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

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

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

Other Health Care Laws and Compliance Requirements

We will also be subject to health care regulation and enforcement by the federal government and the states and foreign governments in which we will conduct our business once our products are approved. The laws that may affect our ability to operate include, but are not limited to: the federal Health Insurance Portability and Accountability Act of 1996 (“HIPAA”), as amended by the Health Information Technology for Economic and Clinical Health Act, which governs the conduct of certain electronic health care transactions and protects the

security and privacy of protected health information. Criminal health care fraud statutes under HIPAA also prohibits persons and entities from knowingly and willfully executing a scheme to defraud any health care benefit program, including private payors, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for health care benefits, items or services; the federal health care programs' Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, in exchange for or to induce either the referral of an individual for, or the purchase, order or recommendation of, any good or service for which payment may be made under federal health care programs such as the Medicare and Medicaid programs; federal false claims laws and civil monetary penalties laws that prohibit, among other things, any person or entity from knowingly presenting, or causing to be presented, a false claim for payment to the federal government, or knowingly making, or causing to be made, a false statement to have a false claim paid; and the Physician Payments Sunshine Act, which requires certain manufacturers of drugs, devices, biologics, and medical supplies for which payment is available under Medicare, Medicaid, or Children's Health Insurance Program to report annually to the U.S. Department of Health and Human Services information related to payments and other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, and ownership and investment interests held by physicians and their immediate family members.

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

Because of the breadth of these laws and the narrowness of available statutory and regulatory exceptions, it is possible that some of our business activities could be subject to challenge under one or more of such laws. If we or our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, individual imprisonment, disgorgement, exclusion of products from reimbursement under U.S. federal or state health care programs, and the curtailment or restructuring of our operations.

Government Regulation Outside of the United States

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

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

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

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

The requirements for conducting clinical trials in Australia, where we anticipate conducting Phase 1 trials for PTG-200 and PTG-300, are as follows:

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

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

The CTN process broadly involves:

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

The CTX process broadly involves:

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

In each case, it is required that:

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

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

Clinical trials involve administering the investigational product to healthy volunteers or patients under the supervision of a qualified principal investigator. The TGA has developed guidelines for a CTN. Under the CTN process, all material relating to the proposed trial is submitted directly to the HREC of each institution at which the trial is to be conducted. An HREC is an independent review committee set up under guidelines of the

Australian National Health and Medical Research Council. The role of an HREC is to ensure the protection of rights, safety and wellbeing of human subjects involved in a clinical trial by, among other things, reviewing, approving and providing continuing review of trial protocols and amendments, and of the methods and material to be used in obtaining and documenting informed consent of the trial subjects. The TGA is formally notified by submission of a CTN application but does not review the safety of the drug or any aspect of the proposed clinical trial. The approving authority of each institution gives the final approval for the conduct of the clinical trial, having due regard to advice from the HREC. Following approval, responsibility for all aspects of the trial conducted under a CTN application remains with the HREC of each investigator's institution.

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

Employees

As of December 31, 2016, we had 35 full-time employees, 27 of whom were in research and development of which 2 hold an M.D. and 10 hold Ph.D. degrees. The remaining 8 employees worked in finance, business development, human resources and administrative support of which 2 hold a Ph.D. None of our employees are represented by a labor union or covered by a collective bargaining agreement. We consider our relationship with our employees to be good.

Corporate and Other Information

Protagonist Pty Limited ("Protagonist Australia") was incorporated in Australia in September 2001. We were incorporated as a Delaware corporation in 2006, under the name Protagonist Therapeutics, Inc., and became the parent of Protagonist Australia pursuant to a transaction in which all of the issued and outstanding capital stock of Protagonist Australia was exchanged for shares of our common stock and Series A preferred stock. Our principal executive offices are located at 521 Cottonwood Drive, Suite 100, Milpitas, California 95035. Our telephone number is (408) 649-7370. 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

Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below, together with the other information included or incorporated by reference in this Annual Report on Form 10-K, including the section of this report titled "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our consolidated financial statements and the related notes. We cannot assure you that any of the events discussed in the risk factors below will not occur. The occurrence of any of the events or developments described below could have a material and adverse impact on our business, results of operations, financial condition, and cash flows and future prospects and, if so, our future prospects would likely be materially and adversely affected. If any of such events were to happen, the trading price of our common stock could decline, and you could lose all or part of your investment. Although we have discussed all known material risks, the risks described below are not the only ones that we may face, and additional risks or uncertainties not known to us or that we currently deem immaterial may also impair our business and future prospects.

Risks Related to Our Financial Position and Capital Requirements

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

We have incurred significant operating losses since our inception in 2006. Our net loss for the years ended December 31, 2016, 2015, and 2014 was approximately $37.2 million, $14.9 million, and $11.1 million, respectively. As of December 31, 2016, we had an accumulated deficit of $64.6 million. Our prior losses, combined with expected future losses, have had and will continue to have an adverse effect on our stockholders' equity and working capital. We expect to continue incurring significant research, development and other expenses related to our ongoing operations and product development, and as a result, we expect to continue incurring losses for the foreseeable future. We also expect these losses to increase as we continue our development of, and seek regulatory approvals for, our peptide-based product candidates.

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

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

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

We are an early clinical-stage biopharmaceutical company with a limited operating history upon which you can evaluate our business and prospects. Biopharmaceutical product development is a highly speculative undertaking and involves a substantial degree of uncertainty. Our operations to date have been limited to developing our technology, undertaking pre-clinical studies and clinical trials of our pipeline candidates, including pre-clinical studies and clinical trial of PTG-100 and pre-clinical studies of PTG-200 and PTG-300, as well as our proprietary technology platform. We successfully filed a CTN in Australia to support our completed Phase 1 clinical trial of PTG-100. We have successfully filed a U.S. IND application to support our ongoing

Phase 2b study of PTG-100 in ulcerative colitis ("UC"). As an early clinical-stage company, we have not yet demonstrated an ability to generate revenue or successfully overcome many of the risks and uncertainties frequently encountered by companies in new and rapidly evolving fields such as biopharmaceutical drug discovery and development. Consequently, the ability to accurately assess our future operating results or business prospects is significantly more limited than if we had a longer operating history or approved products on the market.

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

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

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

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

Our operations have consumed substantial amounts of cash since inception. We conducted a Phase 1 clinical trial of PTG-100 in healthy volunteers and we have initiated a Phase 2b clinical trial of PTG-100 in patients with

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

Based upon our current operating plan and expected expenditures, we believe that our existing cash, cash equivalents, and available-for-sale securities will be sufficient to fund our operations for at least the next 12 months. Our existing capital resources will not be sufficient to enable us to initiate any pivotal clinical trials. Accordingly, we expect that we will need to raise substantial additional funds in the future in order to complete clinical development or commercialize any of our product candidates. Our funding requirements and the timing of our need for additional capital are subject to change based on a number of factors, including:

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

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

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

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

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

Risks Related to Our Business and Industry

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

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

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

- we may not be able to demonstrate that any of our product candidates is safe and effective to the satisfaction of the FDA or comparable foreign regulatory authorities;

- the FDA or comparable foreign regulatory authorities may require additional pre-clinical studies or clinical trials prior to granting approval, which would increase our costs and extend the pre-approval development process;
- the results of our clinical trials may not meet the level of statistical or clinical significance required by the FDA or comparable foreign regulatory authorities for approval;
- the FDA may disagree with the number, design, size, conduct or statistical analysis of one or more of our clinical trials;
- contract research organizations ("CROs") that we retain to conduct clinical trials may take actions outside of our control that materially and adversely impact our clinical trials;
- the FDA or comparable foreign regulatory authorities may disagree with, or not accept, our interpretation of data from our pre-clinical studies and clinical trials;
- the FDA may require development of a costly and extensive risk evaluation and mitigation strategy ("REMS"), as a condition of approval;
- the FDA may identify deficiencies in our manufacturing processes or facilities or those of our third-party manufacturers which would be required to be corrected prior to regulatory approval;
- the success or further approval of competitor products approved in indications in which we undertake development of our product candidates may change the standard of care or change the standard for approval of our product candidate in our proposed indications; and
- the FDA or comparable foreign regulatory authorities may change their approval policies or adopt new regulations.

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

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

Our business and future profitability is substantially dependent on our ability to successfully develop, obtain regulatory approval for and then successfully commercialize our most advanced peptide-based product candidates, PTG-100, which is in an ongoing Phase 2b trial, and PTG-200 and PTG-300, which are in pre-clinical development. We are not permitted to market or promote any of our peptide-based product candidates before we receive regulatory approval from the FDA, the EMA or any other foreign regulatory authority, and we may never receive such regulatory approval for any of our peptide-based product candidates. The time required to obtain approval by the FDA and comparable foreign authorities is unpredictable, typically takes many years following the commencement of clinical trials and depends upon numerous factors, including the substantial discretion of regulatory authorities. Approval policies, regulations and the types and amount of clinical and manufacturing data necessary to gain approval may change during the course of clinical development and may vary among jurisdictions. We have not obtained regulatory approval for any product candidate and it is possible that none of our existing product candidates or any product candidates we have in development or may seek to develop in the future will ever obtain regulatory approval.

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

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

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

In addition, even if we were to obtain regulatory approval, regulatory authorities may approve our product candidates for fewer or more limited indications than what we requested approval for, may include safety warnings or other restrictions that may negatively impact the commercial viability of 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 BLA, a Marketing Authorization Application ("MAA"), or any corresponding drug approval filing to the FDA, the EMA or any comparable foreign authority for any peptide-based product candidate. Further, our product candidates may not receive regulatory approval even if we complete such filings. If we do not receive regulatory approvals for our product candidates, we may not be able to continue our operations.

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

Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical development process. The results of pre-clinical studies and early clinical trials of our product candidates and studies and trials of other products may not be predictive of the

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

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

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

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

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

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

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

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

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

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

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

As part of our strategy to mitigate clinical development risk, we seek to develop peptide-based product candidates against biological targets and pathways which have been identified as addressable by approved or later stage products in development. While we utilize pre-clinical *in vivo* and *in vitro* models as well as clinical

biomarkers to assess potential safety and efficacy early in the candidate selection and development process, this strategy necessarily relies upon clinical data and other results obtained by third parties that may ultimately prove to be inaccurate or unreliable or otherwise not applicable to the indications in which we develop our peptide-based product candidates. We will have to conduct clinical trials to show the safety and efficacy of our peptide-based product candidates against the identified biological targets and pathways to show that our peptide-based product candidates can address the identified mechanism of action shown by these third party results. For example, PTG-100 is an α 4 β 7 integrin antagonist that targets the same target as the currently marketed injectable antibody drug, Entyvio ®, and PTG-200 targets the IL-23 biological pathway, which is a pathway targeted by the currently marketed injectable antibody drug, Stelara ®, approved for treatment of psoriasis and Crohn's disease. If our interpretation of the third party clinical data and results from molecules directed against the same biological target or pathway or our pre-clinical *in vivo* and *in vitro* models prove inaccurate or our assumptions and conclusions about the applicability of our peptide-based product candidates against the same biological targets or pathways are incorrect or inaccurate, then our development efforts may prove longer and more extensive and our research and development strategy and business and operations could be significantly harmed.

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

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

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

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

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

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

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

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

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

We have relied upon and plan to continue to rely upon third party CROs to monitor and manage clinical trials and collect data for our pre-clinical studies and clinical programs. We rely on these parties for execution of our pre-clinical studies and clinical trials, and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that their conduct meets regulatory requirements and that each of our studies and trials is conducted in accordance with the applicable protocol, legal, regulatory and scientific standards, and our reliance on CROs does not relieve us of our regulatory responsibilities. Thus, we and our CROs are required to comply with good clinical practices ("GCPs"), which are regulations and guidelines promulgated by the FDA, the EMA and comparable foreign regulatory authorities for all of our product candidates in clinical development. Regulatory authorities enforce these GCPs through periodic inspections of trial sponsors, principal investigators and trial sites. If we or any of our CROs fail to comply with applicable GCPs, the clinical data generated in our clinical trials may be deemed unreliable and the FDA, EMA or comparable foreign regulatory authorities may not accept the data or require us to perform additional clinical trials before considering our filing for regulatory approval or approving our marketing application. We cannot assure you that upon inspection by a regulatory authority, such regulatory authority will determine that any of our clinical trials complies with GCPs. While we have agreements governing activities of our CROs, we may have limited influence over their actual performance and the qualifications of their personnel conducting work on our behalf. In addition, significant portions of the clinical studies for our peptide-based product candidates are expected to be conducted outside of the United States, which will make it more difficult for us to monitor CROs and perform visits of our clinical trial sites and will force us to rely heavily on CROs to ensure the proper and timely conduct of our clinical trials and compliance with applicable regulations, including GCPs. Failure to comply with applicable regulations in the conduct of the clinical studies for our peptide-based product candidates may require us to repeat clinical trials, which would delay the regulatory approval process.

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

If any of our relationships with these third party CROs terminate, we may not be able to enter into arrangements with alternative CROs or do so on commercially reasonable terms. In addition, our CROs are not our employees, and except for remedies available to us under our agreements with such CROs, we cannot control whether or not they devote sufficient time and resources to our pre-clinical and clinical programs. If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be

replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols, regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our peptide-based product candidates. As a result, our results of operations and the commercial prospects for our peptide-based product candidates would be harmed, our costs could increase substantially and our ability to generate revenue could be delayed significantly.

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

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

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

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

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

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

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

We have not obtained nor have we sought to obtain orphan designation for any product candidates to date, although we believe some of the potential indications of our product candidates could qualify for orphan drug designation and the related benefits if approved for that indication. For example, if PTG-100 or PTG-200 is developed for the treatment of pediatric IBD or PTG-300 for the treatment of iron overload disorders in patients with ß-Thalassemia and possibly HH and SCD, we plan to file and expect to qualify for orphan drug designation with respect to such indication. Even if we obtain such designations, we may not be the first to obtain regulatory approval of a product candidate for the orphan-designated indication due to the uncertainties associated with developing pharmaceutical products. In addition, exclusive marketing rights in the United States may be limited if we seek approval for an indication broader than the orphan-designated indication or may be lost if the FDA later determines that the request for designation was materially defective or if we are unable to assure sufficient quantities of the product to meet the needs of patients with the orphan-designated disease or condition. Further, even if we obtain orphan drug designation exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs with different active moieties may receive and be approved for the same condition, and only the first applicant to receive approval will receive the benefits of marketing exclusivity. Even after an orphan-designated product is approved, the FDA can subsequently approve a later drug with the same active moiety for the same condition if the FDA concludes that the later drug is clinically superior if it is shown to be safer, more effective or makes a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a drug, nor gives the drug any advantage in the regulatory review or approval process. In addition, while we may seek orphan drug designation for our product candidates, we may never receive such designations.

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

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

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

- reductions in the payment of royalties or other payments we believe are due pursuant to the applicable collaboration arrangement;
- actions taken by a partner inside or outside our collaboration which could negatively impact our rights or benefits under our collaboration; or
- unwillingness on the part of a partner to keep us informed regarding the progress of its development and commercialization activities or to permit public disclosure of the results of those activities.

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

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

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

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

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

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

- Infused $\alpha 4 \beta 7$ antibody: Takeda Pharmaceutical Company
- Infused IL-23 and IL-12 antibody: Johnson & Johnson
- Injectable or infused TNF-α antibody: AbbVie, Johnson & Johnson, Amgen, Pfizer, UCB S.A.

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

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

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

- the efficacy and safety of our product candidates, in particular compared to marketed products and products in late-stage development;
- the time it takes for our product candidates to complete clinical development and receive regulatory approval, if at all;
- the ability to commercialize and market any of our product candidates that receive regulatory approval;
- the price of our products, including in comparison to branded or generic competitors;

- whether coverage and adequate levels of reimbursement are available under private and governmental health insurance plans, including Medicare;
- the ability to protect intellectual property rights related to our product candidates;
- the ability to manufacture and sell commercial quantities of any of our product candidates that receive regulatory approval; and
- acceptance of any of our approved product candidates by physicians, payors and other healthcare providers.

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

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

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

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

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

- the efficacy and potential advantages compared to alternative treatments;
- effectiveness of sales and marketing efforts;
- the cost of treatment in relation to alternative treatments;

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

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

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

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

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

Sales of our product candidates outside of the United States will be subject to foreign regulatory requirements governing clinical trials and marketing approval and, to the extent that we retain commercial rights following clinical development, we would plan to seek regulatory approval to commercialize our peptide-based product candidates in the United States, the EU and additional foreign countries. Even if the FDA grants marketing approval for a product candidate, comparable regulatory authorities of foreign countries must also approve the manufacturing and marketing of the product candidates in those countries. Approval procedures vary among jurisdictions and can involve requirements and administrative review periods different from, and greater than, those in the US, including additional pre-clinical studies or clinical trials. In many countries outside the US, a product candidate must be approved for reimbursement before it can be approved for sale in that country. In some cases, the price that we intend to charge for our products is also subject to approval. We may decide to submit an MAA to the EMA for approval in the EEA. As with the FDA, obtaining approval of an MAA from the EMA is a similarly lengthy and expensive process and the EMA has its own procedures for approval of peptide-based product candidates. Even if a product is approved, the FDA or the EMA, as the case may be, may

limit the indications for which the product may be marketed, require extensive warnings on the product labeling or require expensive and time-consuming clinical trials or reporting as conditions of approval. Regulatory authorities in countries outside of the US and the EEA also have requirements for approval of drug candidates with which we must comply prior to marketing in those countries. Obtaining foreign regulatory approvals and compliance with foreign regulatory requirements could result in significant delays, difficulties and costs for us and could delay or prevent the introduction of our products in certain countries. Further, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries and regulatory approval in one country does not ensure approval in any other country, while a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory approval process in others. Also, regulatory approval for any of our peptide-based product candidates may be withdrawn. If we fail to comply with the regulatory requirements in international markets and or receive applicable marketing approvals, our target market will be reduced and our ability to realize the full market potential of our peptide-based product candidates will be harmed and our business will be adversely affected.

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

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

- the federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, receiving, offering, or paying remuneration, directly or indirectly, in cash or in kind, in exchange for or to induce either the referral of an individual for, or the purchase, lease, order or recommendation of, any good, facility, item or service for which payment may be made, in whole or in part, under a federal healthcare programs such as Medicare and Medicaid. A person or entity does not need to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation;
- the federal false claims and civil monetary penalties laws, including the False Claims Act, which impose criminal and civil penalties, including through civil whistleblower or qui tam actions, against individuals or entities for knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false, fictitious, or fraudulent; knowingly making, using, or causing to be made or used, a false record or statement to get a false or fraudulent claim paid or approved by the government; or knowingly making, using, or causing to be made or used, a false record or statement to avoid, decrease or conceal an obligation to pay money to the federal government; in addition, the government may assert that a claim including items and services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act;
- the federal Health Insurance Portability and Accountability Act of 1996 ("HIPAA"), which imposes additional criminal and civil liability for, among other things, willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or making false or fraudulent statements relating to healthcare matters; similar to the federal Anti-Kickback Statute, a person or entity does not need to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation;

- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act ("HITECH"), and their implementing regulations, which also imposes obligations, including mandatory contractual terms, on certain types of people and entities with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal civil monetary penalties statute, which prohibits, among other things, the offering or giving of remuneration to a Medicare or Medicaid beneficiary that the person knows or should know is likely to influence the beneficiary's selection of a particular supplier of items or services reimbursable by a Federal or state governmental program;
- the federal Physician Payment Sunshine Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies for which payment is available under Medicare, Medicaid or the Children's Health Insurance Program (with certain exceptions) to report annually to the government information related to certain payments and other "transfers of value" made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, and requires applicable manufacturers to report annually to the government ownership and investment interests held by the physicians described above and their immediate family members and payments or other "transfers of value" to such physician owners; and
- analogous state and foreign laws and regulations, such as state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by any third-party payor, including commercial insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; and state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; and state and foreign laws governing the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Further, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act (collectively, the "ACA"), among other things, amended the intent requirements of the federal Anti-Kickback Statute and certain criminal statutes governing healthcare fraud. A person or entity can now be found guilty of violating the statute without actual knowledge of the statute or specific intent to violate it. In addition, ACA provided that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act. Moreover, while we do not submit claims and our customers make the ultimate decision on how to submit claims, from time to time, we may provide reimbursement guidance to our customers. If a government authority were to conclude that we provided improper advice to our customers or encouraged the submission of false claims for reimbursement, we could face action against us by government authorities. Any violations of these laws, or any action against us for violation of these laws, even if we successfully defend against it, could result in a material adverse effect on our reputation, business, results of operations and financial condition.

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

The scope and enforcement of each of these laws is uncertain and subject to rapid change in the current environment of healthcare reform, especially in light of the lack of applicable precedent and regulations. Federal

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

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

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

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

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

- an annual, non-tax deductible fee payable by any entity that manufactures or imports specified branded prescription drugs and biologic agents payable to the federal government based on each company's market share of prior year total sales of branded products to certain federal healthcare programs;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program;
- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- extension of manufacturers' Medicaid rebate liability to individuals enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs in certain states;
- a new Medicare Part D coverage gap discount program, in which manufacturers must agree to offer 50% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries under their coverage gap period, as a condition for the manufacturer's outpatient drugs to be covered under Medicare Part D;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program;

- a new requirement to annually report drug samples that manufacturers and distributors provide to physicians; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

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

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

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

Some of the provisions of the ACA have yet to be fully implemented, while certain provisions have been subject to judicial and Congressional challenges. In January 2017, Congress voted to adopt a budget resolution for fiscal year 2017, that while not a law, is widely viewed as the first step toward the passage of legislation that would repeal certain aspects of the Affordable Care Act. Further, on January 20, 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the Affordable Care Act to waive, defer, grant exemptions from, or delay the implementation of any provision of the Affordable Care Act that would impose a fiscal burden on states or a cost, fee, tax, penalty or regulatory burden on individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. Congress also could consider subsequent legislation to replace elements of the Affordable Care Act that are repealed. Thus, the full impact of the Affordable Care Act, or any law replacing elements of it, on our business remains unclear. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our drugs.

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

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

In some countries, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product candidate. In addition, there can be considerable pressure by governments and

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

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

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

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

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

As of December 31, 2016, we had 35 full-time employees, including 27 employees engaged in research and development. As our development and commercialization plans and strategies develop and operate as a public company, we expect to need additional managerial, operational, scientific, sales, marketing, development, regulatory, manufacturing, financial and other resources. Future growth would impose significant added responsibilities on members of management, including:

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

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

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

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

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

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

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

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

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials

and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

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

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

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

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

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

- delay or termination of clinical studies;
- injury to our reputation;

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

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

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

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

- Medical standard of care and diagnostic criteria may differ in foreign jurisdictions, which may impact our ability to enroll and successfully complete trials designed for U.S. marketing;
- efforts to develop an international sales, marketing and distribution organization may increase our expenses, divert our management's attention from the acquisition or development of peptide-based product candidates or cause us to forgo profitable licensing opportunities in these geographies;
- changes in a specific country's or region's political and cultural climate or economic condition;
- unexpected changes in foreign laws and regulatory requirements;
- difficulty of effective enforcement of contractual provisions in local jurisdictions;
- inadequate intellectual property protection in foreign countries;
- trade-protection measures, import or export licensing requirements such as Export Administration Regulations promulgated by the US Department of Commerce and fines, penalties or suspension or revocation of export privileges;

- regulations under the U.S. Foreign Corrupt Practices Act and similar foreign anti-corruption laws;
- the effects of applicable foreign tax structures and potentially adverse tax consequences; and
- significant adverse changes in foreign currency exchange rates which could make the cost of our clinical trials, to the extent conducted outside of the US, more expensive.

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

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

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

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

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

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

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

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

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

Risks Related to Our Intellectual Property

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

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

If the breadth or strength of protection provided by the patent and patent applications we hold, obtain or pursue with respect to our product candidates and technologies is challenged, or if they fail to provide meaningful exclusivity for our product candidates and technologies, it could threaten our ability to commercialize our product candidates and technologies. Several patent applications covering our product candidates and technologies have been filed recently. We cannot offer any assurances about which, if any, patents will issue, the breadth of any such patent, or whether any issued patents will be found invalid and unenforceable or will be threatened by third parties. Any successful opposition to these patents or any other

patents owned by or, if applicable in the future, licensed to us could deprive us of rights necessary for the successful commercialization of any product candidates and technologies that we may develop. Further, if we encounter delays in our clinical trials or in gaining regulatory approval, the period of time during which we could market any of our product candidates under patent protection, if approved, would be reduced. Since patent applications in the United States and most other countries are confidential for a period of time after filing, we cannot be certain that we or our licensors were the first to file any patent application related to our product candidates and technologies. Furthermore, an interference proceeding can be provoked by a third party or instituted by the U.S. Patent and Trademark Office ("PTO") to determine who was the first to invent any of the subject matter covered by the patent claims of our applications. In addition, patents have a limited lifespan. In the United States, the natural expiration of a patent is generally 20 years after it is filed. Various extensions may be available however the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired for a product, we may be open to competition from generic medications.

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

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

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

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

We also seek to preserve the integrity and confidentiality of our data, trade secrets and know-how by maintaining physical security of our premises and physical and electronic security of our information technology systems. Monitoring unauthorized uses and disclosures is difficult, and we do not know whether the steps we

have taken to protect our proprietary technologies will be effective. We cannot guarantee that our trade secrets and other proprietary and confidential information will not be disclosed or that competitors will not otherwise gain access to our trade secrets.

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

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

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

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

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

Interference proceedings provoked by third parties or brought by us, the PTO or any foreign patent authority may be necessary to determine the priority of inventions with respect to our patent or patent applications. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on

commercially reasonable terms, if any license is offered at all. Our defense of litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees.

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

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

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

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

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

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

Under the Hatch-Waxman Act, a pharmaceutical manufacturer may file an abbreviated new drug application, or ANDA, seeking approval of a generic copy of an approved innovator product. Under the Hatch-Waxman Act, a manufacturer may also submit an NDA under section 505(b)(2) that references the FDA's

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

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

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

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

Our commercial success depends in part on our ability to develop, manufacture, market and sell our drug candidates and use our proprietary technologies without infringing or otherwise violating the patents and proprietary rights of third parties. There is a substantial amount of litigation involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, derivation proceedings, post grant reviews, inter partes reviews, and reexamination proceedings before the PTO or oppositions and other comparable proceedings in foreign jurisdictions. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing product candidates, and there may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates and technologies. Third parties, including our competitors may initiate legal proceedings against us alleging that we are infringing or otherwise violating their patent or other intellectual property rights. Given the vast number of patents in our field of technology, we cannot assure you that marketing of our product candidates or practice of our technologies will not infringe existing patents or patents that may be granted in the future. Because patent applications can take many years to issue and may be confidential for 18 months or more after filing, and because pending patent claims can be revised before issuance, there may be applications now pending of which we are unaware that may later result in issued patents that may be infringed by the practice of our peptide therapeutics technology platform or the manufacture, use or sale of our product candidates. If a patent holder believes our product candidates or technologies infringe on its patent, the patent

holder may sue us even if we have received patent protection for our product candidates and technologies. In addition, third parties may obtain patents in the future and claim that our product candidates or technologies infringe upon these patents. If any third-party patents were held by a court of competent jurisdiction to cover the manufacturing process of any of our product candidates, any molecules formed during the manufacturing process or any final product or formulation itself, the holders of any such patents may be able to block our ability to commercialize such product candidate unless we obtained a license under the applicable patents, or until such patents expire. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates or technologies may give rise to claims of infringement of the patent rights of others.

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

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

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

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

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

Because of the expense and uncertainty of litigation, we may conclude that even if a third party is infringing our issued patent, any patents that may be issued on as a result of our pending or future patent applications or

other intellectual property rights, the risk-adjusted cost of bringing and enforcing such a claim or action may be too high or not in the best interest of our company or our shareholders. In such cases, we may decide that the more prudent course of action is to simply monitor the situation or initiate or seek some other non-litigious action or solution.

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

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

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

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

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

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

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

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

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

The PTO and various non-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 will be prosecuted and may also affect patent litigation. The PTO is currently developing regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first to file provisions, did not become effective until March 2013, 18 months after its enactment. Accordingly, it is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business. However, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

Recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. Depending on decisions by the U.S. Congress, the federal courts, and the PTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patent and patents that we might obtain in the future.

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

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

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

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

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

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

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

We may also be subject to claims that former employees, collaborators or other third parties have an ownership interest in our issued patent, any patents issued as a result of our pending or future applications or

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

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

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

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

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

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

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

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

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

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

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

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

- collaborators have significant discretion in determining the efforts and resources that they will apply to collaborations;
- collaborators may not pursue development and commercialization of our product candidates or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in their strategic focus due to the acquisition of competitive products, availability of funding or other external factors, such as a business combination that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial, abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates;
- a collaborator with marketing, manufacturing and distribution rights to one or more products may not commit sufficient resources to or otherwise not perform satisfactorily in carrying out these activities;
- we could grant exclusive rights to our collaborators that would prevent us from collaborating with others;

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

Risks Related to Ownership of our Common Stock

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

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

- any delay in the commencement, enrollment and ultimate completion of clinical trials;
- actual or anticipated results in our clinical trials or those of our competitors;
- positive outcomes, or faster development results than expected, by parties developing peptide-based product candidates that are competitive with our peptide-based product candidates, as well as approval of any such competitive peptide-based product candidates;
- failure to successfully develop commercial-scale manufacturing capabilities;
- unanticipated serious safety concerns related to the use of any of our peptide-based product candidates;
- failure to secure collaboration agreements for our peptide-based product candidates or actual or perceived unfavorable terms of such agreements;
- adverse regulatory decisions;
- changes in the structure of healthcare payment systems;
- changes in laws or regulations applicable to our product candidates, including but not limited to clinical trial requirements for approvals;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our peptide-based product candidates;
- our dependence on third parties, including CROs as well as manufacturers;
- our failure to successfully commercialize any of our peptide-based product candidates, if approved;
- additions or departures of key scientific or management personnel;
- failure to meet or exceed any financial guidance or development timelines that we may provide to the public;

- actual or anticipated variations in quarterly operating results;
- failure to meet or exceed the estimates and projections of the investment community;
- overall performance of the equity markets and other factors that may be unrelated to our operating performance or the operating performance of our competitors, including changes in market valuations of similar companies;
- conditions or trends in the biotechnology and biopharmaceutical industries;
- announcements of significant acquisitions, strategic collaborations, joint ventures or capital commitments by us or our competitors;
- our ability to maintain an adequate rate of growth and manage such growth;
- issuances of debt or equity securities;
- significant lawsuits, including patent or stockholder litigation;
- sales of our common stock by us or our stockholders in the future;
- trading volume of our common stock;
- publication of research reports about us or our industry or positive or negative recommendations or withdrawal of research coverage by securities analysts;
- ineffectiveness of our internal controls;
- general political and economic conditions; and
- effects of natural or man-made catastrophic events.

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

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

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

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

As of December 31, 2016, our executive officers, directors, holders of 5% or more of our capital stock and their respective affiliates beneficially owned approximately 78% of our stock. Therefore, these stockholders will have substantial influence and may be able to determine all matters requiring stockholder approval. For example, these stockholders may be able to control elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This concentration of voting power could, among other things, delay or prevent an acquisition of our company on terms that other stockholders may desire, which in turn could depress our stock price and may prevent attempts by our stockholders to replace or remove the board of directors or management.

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

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

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

Neither we nor our independent registered public accounting firm has performed or was required to perform an evaluation of our internal control over financial reporting in according with Section 404 of the Sarbanes-Oxley Act. We have taken steps to remediate the material weaknesses, including increasing the depth and experience within our accounting and finance organization, and implemented an approval process related to manual journal entries and the related supporting journal entry calculations. In addition, we are continuing to work on designing and implementing additional improved processes and internal controls. While we intend to implement a plan to remediate the material weaknesses, we have not completed the implementation of this plan as of December 31, 2016. Accordingly, we continue to have the material weaknesses as of December 31, 2016. We can give no assurance that our current and planned implementation will remediate this deficiency in internal control or that additional material weaknesses or significant deficiencies in our internal control over financial reporting will not be identified in the future. Our failure to implement and maintain effective internal control over financial reporting could result in errors in our financial statements that could result in a restatement of our financial statements and cause us to fail to meet our reporting obligations.

We are obligated to develop and maintain proper and effective internal controls over financial reporting and any failure to maintain the adequacy of these internal controls may adversely affect investor confidence in our company and, as a result, the value of our common stock.

We will be required, pursuant to Section 404 of the Sarbanes-Oxley Act (Section 404), to furnish a report by management on the effectiveness of our internal control over financial reporting for the year ending December 31, 2017. This assessment will need to include disclosure of any material weaknesses identified by our management in our internal control over financial reporting. Our independent registered public accounting firm will not be required to attest to the effectiveness of our internal control over financial reporting until our first Annual Report required to be filed with the SEC following the date we are no longer an “emerging growth company,” as defined in the Jumpstart Our Business Startups Act of 2012 (the “JOBS Act”). At such time as we are required to obtain auditor attestation, if we then have a material weakness, we would receive an adverse opinion regarding our internal control over financial reporting from our independent registered accounting firm.

We have begun the costly and challenging process of compiling the system and processing documentation necessary to perform the evaluation needed to comply with Section 404, and we may not be able to complete our

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

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

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

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

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

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

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

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

Sales of a substantial number of shares of our common stock in the public market, or the perception that these sales might occur, could depress the market price of our common stock and could impair our ability to raise capital through the sale of additional equity securities. At December 31, 2016, we had outstanding a total of 16,722,280 shares of common stock, notwithstanding any potential exercises of outstanding options. 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 if we need to raise additional capital. The number of our new common stock issued in connection with raising additional capital could constitute a material portion of our then outstanding common stock.

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

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

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

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

As a public company, and particularly after we are no longer an "emerging growth company," we will incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of The NASDAQ Global Market and other applicable securities rules and regulations impose various requirements on public companies. Our management and other personnel will need to devote a substantial amount of time to compliance with these requirements. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly. For example, we expect that

these rules and regulations may make it more difficult and more expensive for us to obtain directors' and officers' liability insurance, which could make it more difficult for us to attract and retain qualified members of our board of directors. We cannot predict or estimate the amount of additional costs we will incur as a public company or the timing of such costs.

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

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

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

During the course of our review and testing, we may identify deficiencies and be unable to remediate them before we must provide the required reports. Furthermore, since we have material weaknesses in our internal controls over financial reporting, we may not detect errors on a timely basis and our financial statements may be materially misstated. We or our independent registered public accounting firm may not be able to conclude on an ongoing basis that we have effective internal control over financial reporting, which could harm our operating results, cause investors to lose confidence in our reported financial information and cause the trading price of our stock to fall. In addition, as a public company we will be required to file accurate and timely quarterly and Annual Reports with the SEC under the Exchange Act. Any failure to report our financial results on an accurate and timely basis could result in sanctions, lawsuits, delisting of our shares from The NASDAQ Global Market or other adverse consequences that would materially harm our business.

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

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

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

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

The trading market for our common stock will be influenced by the research and reports that securities or industry analysts publish about us or our business. In the event one or more of the analysts who cover us

downgrade our stock or publish inaccurate or unfavorable research about our business, our stock price could be adversely affected. If one or more of these analysts cease coverage of our company or fail to publish reports on us regularly, demand for our common stock could decrease, and we could lose visibility in the financial markets, which might cause our stock price and trading volume to decline.

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

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

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

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

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

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

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

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

Provisions in our certificate of incorporation and our bylaws may discourage, delay or prevent a merger, acquisition or other change in control of us that stockholders may consider favorable, including transactions in

which stockholders might otherwise receive a premium for their shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Because our board of directors is responsible for appointing the members of our management team, these provisions could in turn affect any attempt by our stockholders to replace current members of our management team.

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

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

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

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

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

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

We have incurred substantial losses during our history. We do not anticipate generating revenue from sales of products for the foreseeable future, if ever, and we may never achieve profitability. To the extent that we continue to generate taxable losses, unused losses will carry forward to offset future taxable income, if any, until such unused losses expire. Under Section 382 of the Internal Revenue Code of 1986, as amended (the "Code"), if a corporation undergoes an "ownership change" (generally defined as a greater than 50 percentage points change (by value) in its equity ownership over a rolling three-year period), the corporation's ability to use its pre-change net operating loss carryforwards and other pre-change tax attributes to offset its post-change income may be limited. We have not completed our analysis to determine what, if any, impact any prior ownership change has had on our ability to utilize our net operating loss carryforwards. In addition, we may experience ownership changes in the future or subsequent shifts in our stock ownership, some of which are outside our control. As of December 31, 2016, we had federal net operating loss carryforwards of approximately $48.0 million that could be limited if we have experienced, or if in the future we experience, an ownership change, which could have an adverse effect on our future results of operations.

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

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

Item 1B. Unresolved Staff Comments

Not applicable.

Item 2. Properties

We lease approximately 11,372 square feet of office and laboratory space in Milpitas, California, under a lease that expires in April 2018, with options to extend the lease for a period of three years. In March 2017, we entered into a seven year lease for approximately 42,877 square feet of office and laboratory space in Newark, California and intend to relocate our operations to the facility in July 2017. We believe that our existing and new facilities and arrangements are adequate to meet our business needs for at least the next 12 months and that additional space will be available on commercially reasonable terms, if required.

Item 3. Legal Proceedings

From time to time, we may become subject to litigation and claims arising in the ordinary course of business. We are not currently a party to any material legal proceedings and we are not aware of any pending or threatened legal proceeding against us that we believe could have a material adverse effect on our business, operating results, financial condition or cash flows.

Item 4. Mine Safety Disclosures

Not applicable.

PART II

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

Market Information

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

	Prices	
	High	Low
2016		
Third Quarter (from August 11, 2016)	$22.56	$10.02
Fourth Quarter	$26.36	$17.45

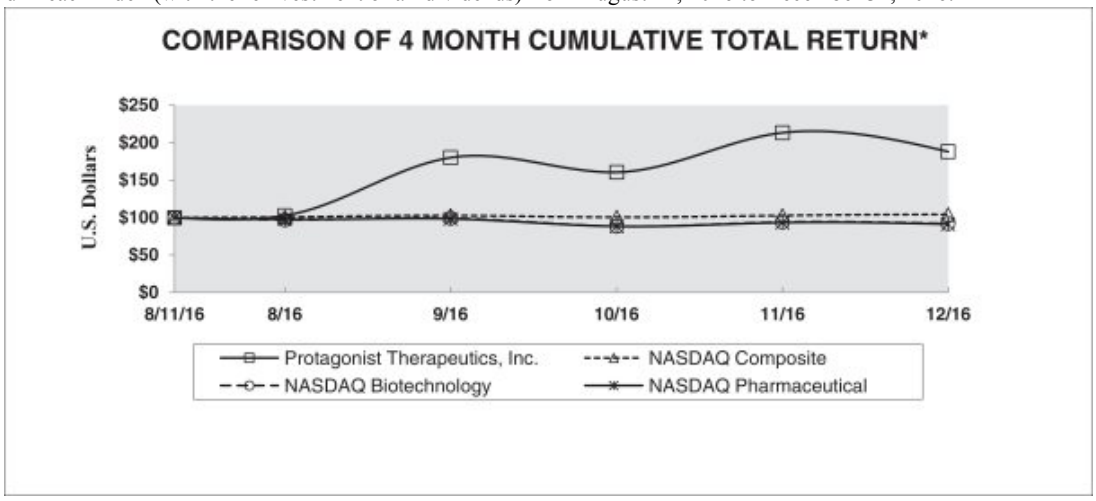
On March 2, 2017, the last reported sale price on The NASDAQ Global Market for our common stock was $14.17.

Holders

As of February 28, 2017, we had approximately 25 record holders of our common stock.

Performance Graph

The following is not deemed "filed" with the Securities and Exchange Commission and is not to be incorporated by reference into any filing we make under the Securities Act of 1933, as amended, whether made before or after the date hereof and irrespective of any general incorporation by reference language in such filing. The graph below matches shows the cumulative total stockholder return assuming the investment on the date specified in each of our common stock, the NASDAQ Composite Index, the NASDAQ Biotechnology Index, and the NASDAQ Pharmaceutical Index. The graph tracks the performance of a $100 investment in our common stock and in each index (with the reinvestment of all dividends) from August 11, 2016 to December 31, 2016.



	8/11/16	8/16	9/16	10/16	11/16	12/16
Protagonist Therapeutics, Inc.	$ 100.00	$ 102.65	$ 180.60	$ 160.68	$ 213.25	$ 187.95
NASDAQ Composite	$ 100.00	$ 101.09	$ 103.02	$ 100.53	$ 103.15	$ 104.35
NASDAQ Biotechnology	$ 100.00	$ 97.26	$ 99.49	$ 88.67	$ 94.20	$ 91.84
NASDAQ Pharmaceutical	$ 100.00	$ 97.62	$ 98.65	$ 88.43	$ 93.61	$ 91.40

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

Recent Sales of Unregistered Securities

(1) In August 2016, upon the closing of our IPO, all 124,374,909 shares of our then-outstanding convertible preferred stock converted into 8,577,571 shares of common stock. The issuance of such shares of common stock was exempt from the registration requirements of the Securities Act, pursuant to Section 3(a)(9) and Section 4(a)(2) of the Securities Act.

(2) From January 1, 2016 through the date of closing of our IPO, we granted stock options to purchase an aggregate of 644,270 shares of common stock at exercise prices ranging between $1.16 and $6.09 to a total of 36 employees, directors and consultants under our 2007 Stock Option and Incentive Plan. From January 1, 2016 through the date of the closing of our IPO, options to purchase an aggregate of 111,501 shares of common stock were exercised.

The offers, sales, and issuances of the securities described in paragraph (2) above were deemed to be exempt from registration under the Securities Act in reliance on Rule 701 thereunder as offers and sales of securities pursuant to certain compensatory benefit plans and contracts relating to compensation in compliance with Rule 701.

Issuer Purchases of Equity Securities

None.

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.

Initial Public Offering

Use of Proceeds

On August 10, 2016, our registration statements on Form S-1 (File Nos. 333-212476 and 333-213071) relating to the IPO became effective. The IPO closed on August 16, 2016 at which time we issued 7,500,000 shares of our common stock at an initial offering price of $12.00 per share. On September 9, 2016, we issued an additional of 252,972 shares of common stock at a price of $12.00 per share following the underwriters' exercise of their option to purchase additional shares. We received an aggregate of $83.6 million in cash, net of underwriting discounts and commissions, and after deducting offering costs paid by us. None of the expenses associated with the IPO were paid to directors, officers, persons owning 10% or more of any class of equity securities, or to their associates, or to our affiliates.

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

Item 6. Selected Consolidated Financial Data

The following selected consolidated statement of operations data for the years ended December 31, 2016, 2015 and 2014 and the consolidated balance sheet data as of December 31, 2016 and 2015 are derived from our audited consolidated financial statements that are included elsewhere in this report. The selected consolidated balance sheet data at December 31, 2014 has 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,		
	2016	2015	2014
	(In thousands, except for share and per share data)		
Consolidated Statement of Operations Data:			
Operating expenses:			
Research and development	$ 25,705	$ 11,831	$ 7,459
General and administrative	6,961	2,963	1,860
Total operating expenses	32,666	14,794	9,319
Loss from operations	(32,666)	(14,794)	(9,319)
Interest income	242	19	16
Change in fair value of redeemable convertible preferred stock tranche and warrant liabilities	(4,719)	(83)	(1,769)
Other expense	(34)	—	—
Net loss	$ (37,177)	$ (14,858)	$ (11,072)
Net loss attributable to common stockholders	$ (37,735)	$ (14,933)	$ (11,218)
Net loss per share attributable to common stockholders, basic and diluted	$ (5.80)	$ (59.32)	$ (49.38)
Weighted-average shares used to compute net loss per share attributable to common stockholders, basic and diluted	6,501,796	251,717	227,197

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

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

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

Overview

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

PTG-100 is a potential first-in-class oral, alpha-4-beta-7 (" α 4 β 7") integrin-specific antagonist peptide product candidate which is currently being evaluated in a global Phase 2b study that is anticipated to enroll approximately 260 patients at about 100 clinical sites. We anticipate completing this trial in the second half of 2018. Our second lead product candidate, PTG-200, is a potential first-in-class oral Interleukin-23 receptor ("IL-23R") antagonist being developed initially for moderate-to-severe CD. Interleukin-23 is a protein produced by white blood cells that regulates inflammatory and immune functions. PTG-200 is currently in Investigational New Drug ("IND") enabling studies, and we plan to initiate a Phase 1 clinical trial in 2017.

Our novel peptides have potential applicability in a wide range of therapeutic areas in addition to GI diseases. Our first product candidate beyond IBD is PTG-300, an injectable hepcidin mimetic, which is currently in pre-clinical development. We plan to complete pre-clinical IND-enabling studies in PTG-300 in the first half of 2017 and complete a Phase 1 study in healthy normal volunteers by the end of 2017. PTG-300 has potential utility for the treatment of iron overload disorders, such as transfusion-dependent ß-Thalassemia, hereditary hemochromatosis ("HH") and sickle cell disease ("SCD"), each of which may qualify for orphan designation.

We are currently researching additional potential oral and injectable peptide-based product candidates for a range of conditions including, but not restricted to GI diseases.

We have not generated any revenue from product sales, and we do not currently have any products approved for commercialization. We have never been profitable and have incurred net losses in each year since inception. Our net losses were $37.2 million, $14.9 million and $11.1 million for the years ended December 31, 2016, 2015 and 2014, respectively. As of December 31, 2016, we had an accumulated deficit of $64.6 million. Substantially all of our net losses have resulted from costs incurred in connection with our research and development programs and from general and administrative costs associated with our operations.

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

Components of Our Results of Operations

Research and Development Expenses

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

Research and development expenses consist primarily of the following:

- expenses incurred under agreements with clinical study sites that conduct research and development activities on our behalf;
- employee-related expenses, which include salaries, benefits and stock-based compensation;
- laboratory vendor expenses related to the preparation and conduct of preclinical, 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
- facilities and other allocated expenses, which include expenses for rent and maintenance of facilities, depreciation and amortization expense and other supplies.

We recognize the funds from grants under government programs as a reduction of research and development expense when the related research costs are incurred. In addition, we recognize the funds related to our Australian research and development tax incentives that are not subject to refund provisions as a reduction of research and development expense. The amounts are determined on a cost reimbursement basis and as the incentive is related to our research and development expenditures and is non-refundable regardless of whether any Australian tax is owed, the amounts have been recorded as a reduction of research and development expenses. These Australian research and development tax incentives are recognized when there is reasonable assurance that the incentive will be received, the relevant expenditure has been incurred and the amount of the consideration can be reliably measured. As of December 31, 2016, the Australian overseas finding research and development tax incentives are no longer deemed to be at risk of clawback as less than 50% of our research and development expenditures under the program were incurred overseas. As a result we have recognized the amounts received for 2014 and 2015 and the amount expected to be received for 2016 qualified expenditures as a reduction of research and development expense during the year ended December 31, 2016.

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

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

	Year Ended December 31,		
	2016	2015	2014
		(In thousands)	
Clinical development expense — PTG-100	$17,988	$ 1,563	$ —
Discovery research expense	11,849	11,159	8,036
Less: Reimbursement of expenses under grants and incentives	(4,132)	(891)	(577)
Total research and development expenses	$25,705	$11,831	$7,459

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

General and Administrative Expenses

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

Interest Income

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

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

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

In connection with our Series B and Series C redeemable convertible preferred stock financings we were obligated to sell additional shares of Series B and Series C redeemable convertible preferred stock in subsequent closings, in each case, contingent upon the achievement of certain development milestones or upon the approval of the investors. We recorded this redeemable convertible preferred stock tranche liability incurred as a derivative financial instrument liability at the fair value on the date of issuance, and we remeasured the liability on each subsequent balance sheet date.

We issued the shares under our Series B obligation in August 2014, and accordingly, we no longer have an obligation as of that date. In March 2016, upon closing of the second tranche of the Series C redeemable

convertible preferred stock, the fair value of the tranche liability was remeasured and the liability was reclassified to redeemable convertible preferred stock.

In addition, in connection with the issuance of our Series B redeemable convertible preferred stock financing, we issued freestanding warrants to purchase shares of Series B redeemable convertible preferred stock. We account for these warrants as a liability in our consolidated financial statements because the underlying instrument into which the warrants are exercisable contains redemption provisions that are outside our control. Upon the exercise of warrants in April 2016, the fair value of the redeemable convertible preferred stock warrant liability was remeasured and the liability was reclassified to redeemable convertible preferred stock. The remaining unexercised warrants expired in May 2016 and accordingly, are no longer subject to remeasurement.

Critical Accounting Policies and Estimates

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

Accrued Research and Development Costs

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

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

Stock-Based Compensation

We recognize compensation costs related to stock options granted to employees based on the estimated fair value of the awards on the date of grant, net of estimated forfeitures. We estimate the fair value, and the resulting

stock-based compensation expense, using the Black-Scholes option-pricing model. The estimated fair value of the stock-based awards is generally recognized on a straight-line basis over the requisite service period, which is generally the vesting period of the respective awards.

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

Expected Term — Our expected term represents the period that our stock-based awards are expected to be outstanding and is determined using the simplified method (based on the mid-point between the vesting date and the end of the contractual term). We have very limited historical information to develop reasonable expectations about future exercise patterns and post-vesting employment termination behavior for our stock option grants.

Expected Volatility —Prior to our IPO in August 2016, we were privately held and did not have any trading history for our common stock, the expected volatility was estimated based on the average volatility for comparable publicly traded biopharmaceutical companies over a period equal to the expected term of the stock option grants. The comparable companies were chosen based on their similar size, stage in the life cycle, or area of specialty. We will continue to apply this process until a sufficient amount of historical information regarding the volatility of our own stock price becomes available.

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

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

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

For the years ended December 31, 2016, 2015, and 2014, stock-based compensation expense was $2.1 million, $99,000 and $42,000, respectively. As of December 31, 2016, we had $12.6 million of total unrecognized stock-based compensation costs, net of estimated forfeitures, which we expect to recognize over a weighted-average period of 3.12 years.

Historically, for all periods prior to our IPO in August 2016, the fair values of the shares of common stock underlying our share-based awards were estimated on each grant date by our board of directors. In order to determine the fair value of our common stock underlying option grants, our board of directors considered, among other things, contemporaneous valuations of our common stock prepared by an unrelated third-party valuation firm in accordance with the guidance provide by the American Institute of Certified Public Accountants Practice Guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation* . Given the absence of a public trading market for our common stock, our board of directors exercised reasonable judgment and considered a number of objective and subjective factors to determine the best estimate of the fair value of our common stock, including our stage of development; progress of our research and development efforts; the rights, preferences and privileges of our preferred stock relative to those of our common stock; equity market conditions affecting comparable public companies and the lack of marketability of our common stock.

For stock options granted after the completion of the IPO, our board of directors determined the fair value of each share of underlying common stock based on the closing price of our common stock as reported on the date of grant.

Income Taxes

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

As of December 31, 2016, our total gross deferred tax assets were $24.0 million. Due to our lack of earnings history and uncertainties surrounding our ability to generate future taxable income, the net deferred tax assets have been fully offset by a valuation allowance. The deferred tax assets were primarily comprised of federal and state tax net operating loss and tax credit carryforwards. As of December 31, 2016, our net operating loss carryforwards for federal income tax purposes of $48.0 million which are available to offset future taxable income, if any, through 2033 and net operating loss carryforwards for state income tax purposes of approximately $37.7 million which are available to offset future taxable income, if any, through 2033. As of December 31, 2016, we also had accumulated Australian tax losses of $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 of 1986 (Code), and similar state provisions. These ownership change limitations may limit the amount of net operating loss carryforwards and other tax attributes that can be utilized annually to offset future taxable income and tax, respectively. In general, an "ownership change" as defined by Section 382 of the Code results from a transaction or series of transactions over a three-year period resulting in an ownership change of more than 50 percentage points (by value) of the outstanding stock of a company by certain stockholders. Since our formation, we have raised capital through the issuance of capital stock on several occasions, which separately or combined with the purchasing stockholders' subsequent disposition of those shares, may have resulted in such ownership changes, or could result in ownership changes in the future.

Results of Operations

Comparison of the year ended December 31, 2016 and 2015

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

* *Percentage not meaningful*

Research and Development Expenses

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

General and Administrative Expenses

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

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

Change in fair value of redeemable convertible preferred stock tranche liability and warrant liabilities increased from a charge of $0.1 million for the year ended December 31, 2015 to a charge of $4.7 million for the year ended December 31, 2016. The change was due to the fair value remeasurement of the outstanding mark to market liabilities as the fair value increased in 2016.

Comparison of the years ended December 31, 2015 and 2014

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

Research and Development Expenses

Research and development expenses increased $4.4 million, or 59%, from $7.5 million for the year ended December 31, 2014 to $11.8 million for the year ended December 31, 2015. The increase was due to an increase

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

General and Administrative Expenses

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

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

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

Liquidity and Capital Resources

Liquidity and Capital Expenditures

As of December 31, 2016, we had $87.7 million of cash, cash equivalents and available-for-sale securities and an accumulated deficit of $64.6 million. In August 2016, we completed our IPO of our common stock pursuant to which we issued 7,500,000 shares of our common stock at a price of $12.00 per share. In September 2016, we issued an additional 252,972 shares of common stock at a price of $12.00 per share following the underwriters' exercise of their option to purchase additional shares. We have received an aggregate of $83.6 million in cash, net of underwriting discounts and commissions and after deducting offering costs paid by us.

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

We believe, based on our current operating plan and expected expenditures, that our existing cash, cash equivalents, and available-for-sale securities will be sufficient to meet our anticipated operating and capital expenditure requirements for at least the next 12 months. 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 preclinical and clinical trials are successful, or our other product candidates enter clinical trials or advance beyond the discovery stage, we will need to raise additional capital in order to further advance our product candidates towards regulatory approval. We will continue to require additional financing to advance our current product candidates through clinical development, to develop, acquire or in-license other potential product candidates and to fund operations for the foreseeable future. We will continue to seek funds through equity or debt financings, collaborative or other arrangements with corporate sources, or through other sources of

financing. We anticipate that we will need to raise substantial additional capital, the requirements of which will depend on many factors, including:

- the progress, timing, scope, results and costs of our preclinical studies and clinical trials for our product candidates, including the ability to enroll patients in a timely manner for our clinical trials;
- the costs of obtaining clinical and commercial supplies and any other product candidates we may identify and develop;
- our ability to successfully commercialize the product candidates we may identify and develop;
- the manufacturing, selling and marketing costs associated with our lead product candidates and any other product candidates we may identify and develop, including the cost and timing of expanding our sales and marketing capabilities;
- the amount and timing of sales and other revenues from our lead product candidates and any other product candidates we may identify and develop, including the sales price and the availability of adequate third-party reimbursement;
- the cash requirements of any future acquisitions or discovery of product candidates;
- the time and cost necessary to respond to technological and market developments;
- the extent to which we may acquire or in-license other product candidates and technologies;
- our ability to attract, hire and retain qualified personnel; and
- the costs of maintaining, expanding and protecting our intellectual property portfolio.

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

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

	Year Ended December 31,		
	2016	2015	2014
		(In thousands)	
Cash used in operating activities	$ (29,972)	$(14,385)	$(7,743)
Cash used in investing activities	(59,328)	(8,264)	(299)
Cash provided by financing activities	106,307	17,419	9,003

Cash Flows from Operating Activities

Cash used in operating activities for the year ended December 31, 2016 was $30.0 million, consisting of a net loss of $37.2 million and a net change of $0.1 million in our net operating assets and liabilities, which were offset by non-cash charges of $7.3 million. The non-cash charges were primarily comprised of $4.2 million for the change in fair value associated with redeemable convertible preferred stock tranche liability, $2.1 million for

stock-based compensation, $0.5 million for the change in fair value of convertible preferred stock warrant liability, and $0.3 million for depreciation and amortization expense. The change in our net operating assets and liabilities was due primarily to an increase of $1.8 million in prepaid and other current assets related to advance payments of costs for research activities during the current period and an increase of $1.6 million in the receivable related to the Australian research and development tax incentives, offset by a $3.3 million increase in our accounts payable and accrued expenses and other payables related to an increase in research and development activities.

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

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

Cash Flows from Investing Activities

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

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

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

Cash Flows from Financing Activities

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

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

Contractual Obligations and Other Commitments

The following table summarizes our contractual obligations as of December 31, 2016:

	Payments Due by Period				
Contractual Obligations:	**Less Than 1 Year**	**1 to 3 Years**	**3 to 5 Years**	**More Than 5 Years**	**Total**
			(In thousands)		
Operating lease obligations	$ 368	$ 87	$ —	$ —	$455
Total contractual obligations	$ 368	$ 87	$ —	$ —	$455

In March 2017, we entered into a lease agreement for a new office and laboratory space in Newark, California to relocate our operations to a larger facility. The lease commencement date is July 1, 2017 and the lease expires on June 30, 2024. The aggregate minimum lease payments under the lease agreement will be approximately $13.4 million, and we are providing the landlord with a security deposit of $450,000.

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

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

Off-Balance Sheet Arrangements

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

Recent Accounting Pronouncements

In August 2014, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("ASU") No. 2014-15, *Disclosure of Uncertainties About an Entity's Ability to Continue as a Going Concern* .

ASU 2014-15 requires management to perform interim and annual assessments of an entity's ability to continue as a going concern within one year of the date the financial statements are issued and provides guidance on determining when and how to disclose going concern uncertainties in the financial statements. Certain disclosures will be required if conditions give rise to substantial doubt about an entity's ability to continue as a going concern. ASU 2014-15 applies to all entities and is effective for annual and interim reporting periods ending after December 15, 2016, with early adoption permitted. We adopted this standard effective December 31, 2016, and there was no impact related to the disclosures in our consolidated financial statements.

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

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

In March 2016, the FASB issued ASU No. 2016-09 Compensation-Stock Compensation (Topic 718) Improvements to Employee Share-Based Payment Accounting, which is intended to simplify several aspects of the accounting for employee share-based payment transactions, including the income tax consequences, the determination of forfeiture rates, classification of awards as either equity or liabilities, and classification on the statement of cash flows. This ASU is effective for fiscal years and interim periods within those years beginning after December 15, 2016 and early adoption is permitted. We are currently evaluating the impact that the adoption of ASU 2016-09 will have on our consolidated financial statements and related disclosures.

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 ASU is effective for fiscal years and interim periods within those years beginning after December 15, 2019 and early adoption is permitted for fiscal years and interim periods within those years beginning after December 15, 2018. We are currently evaluating the impact of this new guidance.

In August 2016, the FASB issued ASU No. 2016-15, *Statement of Cash Flows (Topic 230) – Classification of Certain Cash Receipts and Cash Payments* , which clarifies the classification of certain cash receipts and cash payments in the statements of cash flow to eliminate the diversity in practice related to eight specific cash flow issues. This ASU is effective for fiscal years and interim periods within those years beginning after December 15, 2017, with early adoption permitted. We are currently evaluating the impact of this new guidance.

In November 2016, the FASB issued ASU No. 2016-18, *Statement of Cash Flows (Topic 230) – Restricted Cash,* which requires the presentation of changes in restricted cash or restricted cash equivalents on the statement of cash flows. This ASU is effective for the fiscal years and interim periods within those years beginning after December 15, 2017, with early adoption permitted. We are currently evaluating the impact of this new guidance.

Item 7A. Quantitative and Qualitative Disclosures about Market Risk

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

We had $87.7 million and $11.9 million in cash, cash equivalents and available-for-sale securities as of December 31, 2016 and December 31, 2015, respectively. Cash and cash equivalents consist of cash, money market funds, commercial paper, and government bonds. Available-for-sale securities consist of corporate bonds, commercial paper, and government bonds. Short-term available-for-sale securities have maturities less than 365 days as of the balance sheet date. Long-term available-for-sale securities have maturities greater than 365 days as of the balance sheet date. Such interest earning instruments carry a degree of interest rate risk; however, historical fluctuations in interest income have not been material. We had no outstanding debt as of December 31, 2016.

Approximately $1.9 million and $0.6 million of our cash balance was located in Australia as of December 31, 2016 and December 31, 2015, respectively. Our expenses, except those related to our Australian operations, are generally denominated in U.S. dollars. For our operations in Australia, the majority of the expenses are denominated in Australian dollars. To date, we have not had a formal hedging program with respect to foreign currency, but we may do so in the future if our exposure to foreign currency should become more significant. A 10% increase or decrease in current exchange rates would not have a material effect on our consolidated financial results.

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.

In our opinion, the accompanying consolidated balance sheets and the related consolidated statements of operations, comprehensive loss, redeemable convertible preferred stock and stockholders' equity (deficit), and of cash flows present fairly, in all material respects, the financial position of Protagonist Therapeutics, Inc. and its subsidiary as of December 31, 2016 and 2015, and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2016 in conformity with accounting principles generally accepted in the United States of America. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits. We conducted our audits of these financial statements in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

/s/ PricewaterhouseCoopers LLP

San Jose, California
March 7, 2017

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

	December 31, 2016	December 31, 2015
Assets		
Current assets:		
Cash and cash equivalents	$ 21,084	$ 4,055
Restricted cash	10	10
Available-for-sale securities - current	56,515	7,868
Research and development tax incentive receivable	2,241	715
Prepaid expenses and other current assets	3,394	1,558
Total current assets	83,244	14, 206
Property and equipment, net	562	609
Available-for-sale securities - noncurrent	10,150	—
Other assets	34	30
Total assets	$ 93,990	$ 14,845
Liabilities, Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit)		
Current liabilities:		
Accounts payable	$ 1,163	$ 1,247
Accrued expenses and other payables	5,272	1,879
Total current liabilities	6,435	3,126
Redeemable convertible preferred stock tranche liability	—	1,643
Redeemable convertible preferred stock warrant liability	—	480
Total liabilities	6,435	5,249
Commitments and contingencies		
Redeemable convertible preferred stock, $0.00001 par value: no shares and 126,374,911 shares authorized as of December 31, 2016 and 2015, respectively; no shares and 77,185,117 shares issued and outstanding as of December 31, 2016 and 2015, respectively	—	36,996
Stockholders' equity (deficit):		
Preferred stock, $0.00001 par value, 10,000,000 and no shares authorized as of December 31, 2016 and 2015, respectively; and no shares issued and outstanding as of December 31, 2016 and 2015	—	—
Common stock, $0.00001 par value, 90,000,000 and 160,000,000 shares authorized as of December 31, 2016 and, 2015, respectively; 16,722,280 and 272,409 shares issued and outstanding as of December 31, 2016 and 2015, respectively	—	—
Additional paid-in capital	152,393	118
Accumulated other comprehensive loss	(245)	(102)
Accumulated deficit	(64,593)	(27,416)
Total stockholders' equity (deficit)	87,555	(27,400)
Total liabilities, redeemable convertible preferred stock and stockholders' equity (deficit)	$ 93,990	$ 14,845

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

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

	Year Ended December 31,		
	2016	2015	2014
Operating expenses:			
Research and development	$ 25,705	$ 11,831	$ 7,459
General and administrative	6,961	2,963	1,860
Total operating expenses	32,666	14,794	9,319
Loss from operations	(32,666)	(14,794)	(9,319)
Interest income	242	19	16
Change in fair value of redeemable convertible preferred stock tranche and warrant liabilities	(4,719)	(83)	(1,769)
Other expense	(34)	—	—
Net loss	$ (37,177)	$ (14,858)	$ (11,072)
Net loss attributable to common stockholders	$ (37,735)	$ (14,933)	$ (11,218)
Net loss per share attributable to common stockholders, basic and diluted	$ (5.80)	$ (59.32)	$ (49.38)
Weighted-average shares used to compute net loss per share attributable to common stockholders, basic and diluted	6,501,796	251,717	227,197

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,		
	2016	2015	2014
Net loss	$(37,177)	$(14,858)	$(11,072)
Other comprehensive loss:			
(Loss) gain on translation of foreign operations	(76)	3	(54)
Unrecognized loss on available-for-sale securities	(67)	(5)	—
Comprehensive loss	$(37,320)	$(14,860)	$(11,126)

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

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

	Redeemable Convertible Preferred Stock		Common Stock		Additional Paid-In Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount				
Balance at December 31, 2013	24,037,500	$ 9,122	226,009	$ —	$ 135	$ (46)	$ (1,483)	$ (1,394)
Issuance of Series B redeemable convertible preferred stock	18,000,000	9,000	—	—	—	—	—	—
Settlement of fair value of series B redeemable convertible preferred stock tranche liability	—	2,308	—	—	—	—	—	—
Accretion of redeemable convertible preferred stock to redemption value	—	146	—	—	(143)	—	(3)	(146)
Stock-based compensation expense	—	—	—	—	42	—	—	42
Issuance of common stock upon the exercise of options	—	—	2,548	—	3	—	—	3
Other comprehensive loss	—	—	—	—	—	(54)	—	(54)
Net loss	—	—	—	—	—	—	(11,072)	(11,072)
Balance at December 31, 2014	42,037,500	20,576	228,557	—	37	(100)	(12,558)	(12,621)
Issuance of Series C redeemable convertible preferred stock, net of issuance costs of $138 and reclassification of $1,017 to redeemable convertible preferred stock tranche liability	35,147,617	16,345	—	—	—	—	—	—
Accretion of redeemable convertible preferred stock to redemption value	—	75	—	—	(75)	—	—	(75)
Stock-based compensation expense	—	—	—	—	99	—	—	99
Issuance of common stock upon the exercise of options	—	—	43,852	—	57	—	—	57
Other comprehensive loss	—	—	—	—	—	(2)	—	(2)
Net loss	—	—	—	—	—	—	(14,858)	(14,858)
Balance at December 31, 2015	77,185,117	36,996	272,409	—	118	(102)	(27,416)	(27,400)
Issuance of Series C redeemable convertible preferred stock, net of issuance costs	45,189,794	22,488	—	—	—	—	—	—
Settlement of fair value of redeemable convertible preferred stock tranche liability	—	5,837	—	—	—	—	—	—
Exercise of redeemable convertible preferred stock warrant liability	1,999,998	1,025	—	—	—	—	—	—
Accretion of redemption of convertible preferred stock to redemption value	—	558	—	—	(558)	—	—	(558)
Conversion of redeemable convertible preferred stock to common stock at closing of initial public offering	(124,374,909)	(66,904)	8,577,571	—	66,904	—	—	66,904
Issuance of common stock upon initial public offering, net of issuance costs	—	—	7,752,972	—	83,648	—	—	83,648
Stock-based compensation expense	—	—	—	—	2,130	—	—	2,130
Issuance of common stock upon the exercise of options	—	—	119,328	—	151	—	—	151
Other comprehensive loss	—	—	—	—	—	(143)	—	(143)
Net loss	—	—	—	—	—	—	(37,177)	(37,177)
Balance at December 31, 2016	—	$ —	16,722,280	$ —	$ 152,393	$ (245)	$ (64,593)	$ 87,555

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,		
	2016	2015	2014
CASH FLOWS FROM OPERATING ACTITIVIES			
Net loss	$ (37,177)	$ (14,858)	$ (11,072)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	317	247	258
Loss on disposal of property and equipment	34	—	—
Amortization of premium on available-for-sale securities	117	(8)	—
Stock-based compensation	2,130	99	42
Change in fair value associated with redeemable convertible preferred stock tranche liability	4,194	626	897
Change in fair value of redeemable convertible preferred stock warrant liability	525	(543)	872
Changes in operating assets and liabilities:			
Research and development tax credit receivable	(1,588)	(192)	259
Prepaid expenses and other current assets	(1,800)	(1,502)	604
Other assets	(4)	(30)	—
Accounts payable	(115)	898	179
Accrued expenses and other payables	3,395	878	218
Net cash used in operating activities	(29,972)	(14,385)	(7,743)
CASH FLOWS FROM INVESTING ACTIVITIES			
Purchase of available-for-sale securities	(73,169)	(7,865)	—
Purchase of property and equipment	(379)	(399)	(299)
Proceeds from maturities of available-for-sale securities	14,188	—	—
Proceeds from sale of property and equipment	32	—	—
Net cash used in investing activities	(59,328)	(8,264)	(299)
CASH FLOWS FROM FINANCING ACTIVITIES			
Proceeds from issuance of redeemable convertible preferred stock, net of issuance costs	22,488	17,362	9,000
Proceeds from issuance of redeemable convertible preferred stock upon exercise of preferred stock warrant liability	20	—	—
Proceeds from issuance of common stock upon exercise of stock options	151	57	3
Proceeds from issuance of common stock upon initial public offering, net of issuance costs	83,648	—	—
Net cash provided by financing activities	106,307	17,419	9,003
Effect on exchange rate changes on cash and cash equivalents	22	(39)	(97)
Net increase (decrease) in cash and cash equivalents	17,029	(5,269)	864
Cash and cash equivalents, beginning of year	4,055	9,324	8,460
Cash and cash equivalents, end of year	$ 21,084	$ 4,055	$ 9,324
SUPPLEMENTAL DISCLOSURES OF NON-CASH FINANCING INFORMATION:			
Settlement of fair value of redeemable convertible preferred stock liability	$ 5,837	$ —	$ 2,308
Tranche liability in connection with the Series C redeemable convertible preferred stock financing	$ —	$ 1,017	$ —
Accretion of redeemable convertible preferred stock	$ 558	$ 75	$ 146
Conversion of redeemable convertible preferred stock to common stock at closing of initial public offering	$ 66,904	$ —	$ —
Reclassification of preferred stock warrant liability to equity	$ 1,005	$ —	$ —
Purchase of property and equipment in accounts payable	$ 21	$ —	$ —

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

PROTAGONIST THERAPEUTICS, INC.
Notes to Consolidated Financial Statements

1. Organization and Description of Business

Protagonist Therapeutics, Inc. (the "Company") was incorporated in the state of Delaware on August 22, 2006 and is headquartered in Milpitas, California. The Company is a clinical-stage biopharmaceutical company with a proprietary peptide technology platform focused on discovering and developing new chemical entities to address significant unmet medical needs.

Protagonist Pty Ltd is a wholly-owned subsidiary located in Brisbane, Australia. The Company manages its operations as a single operating segment.

Reverse Stock Split

In July 2016, the Company's board of directors approved an amendment to the Company's amended and restated certificate of incorporation to effect a reverse split of the Company's issued and outstanding common stock at a 1-for-14.5 ratio, which was effected on August 1, 2016. The par value and authorized shares of common stock and convertible preferred stock were not adjusted as a result of the reverse split. All issued and outstanding common stock, options to purchase common stock and per share amounts contained in the consolidated financial statements have been retroactively adjusted to reflect the reverse stock split for all periods presented. The consolidated financial statements have also been retroactively adjusted to reflect a proportional adjustment to the conversion ratio for each series of preferred stock in connection with the reverse stock split.

Initial Public Offering

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

Liquidity

The Company has incurred net losses from operations since inception and has an accumulated deficit of $64.6 million as of December 31, 2016. The Company's ultimate success depends on the outcome of its research and development activities. The Company expects to incur additional losses and negative cash flows for the foreseeable future and it anticipates the need to raise additional capital to fully implement its business plan. The Company intends to raise such capital through the issuance of additional equity and/or strategic alliances with partner companies. As of December 31, 2016, the Company had $87.7 million of cash, cash equivalents and available-for-sale securities and management believes the existing cash, cash equivalents and available-for-sale securities will be sufficient to meet the Company's anticipated operating and capital expenditure requirements.

2. Summary of Significant Accounting Policies

Basis of Presentation and Consolidation

The accompanying consolidated financial statements include the accounts of the Company and its wholly owned subsidiary, Protagonist Pty Ltd and have been prepared in conformity with accounting principles generally accepted in the United States of America (U.S. GAAP). All intercompany balances and transactions have been eliminated in consolidation.

The financial statements of Protagonist Pty Ltd use the Australian dollar as the functional currency since the majority of expense transactions occur in such currency. Gains and losses from foreign currency transactions were not material for all periods presented. The re-measurement from Australian dollar to U.S. dollars is outlined below:

a. Equity accounts, except for the change in retained earnings during the year, have been translated using historical exchange rates.

b. All other Australian dollar denominated assets and liabilities as of December 31, 2016 and 2015 have been translated using the year-end exchange rate.

c. The consolidated statements of operations have been translated at the weighted average exchange rates in effect during each year, except for depreciation, which has been translated at historical exchange rates.

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

Use of Estimates

The preparation of the consolidated financial statements in conformity with U.S. 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 accruals for research and development activities, fair value of redeemable convertible preferred stock tranche liability, fair value of redeemable convertible preferred stock warrant liability, fair value of common stock, stock-based compensation and income taxes. Management bases these estimates on historical and anticipated results, trends, and various other assumptions that the Company believes are reasonable under the circumstances, including assumptions as to future events. Actual results may differ from those estimates.

Concentrations of Credit Risk

Financial instruments that potentially subject the Company to a concentration of credit risk consist of cash, cash equivalents and available-for-sale securities. Substantially all the Company's cash is held by one financial institution that management believes is of high credit quality. Such deposits may, at times, exceed federally insured limits.

Cash Equivalents

Cash equivalents that are readily convertible to cash are stated at cost, which approximates fair value. The Company considers all highly liquid investments purchased with an original maturity of three months or less to be cash equivalents. Cash equivalents consist of amounts invested in money market funds, commercial paper and government bonds.

Restricted Cash

Restricted cash consisted of cash balances primarily held as security in connection with the Company's corporate credit card.

Available-for-Sale Securities

All marketable securities have been classified as "available-for-sale" and are carried at estimated fair value as determined based upon quoted market prices or pricing models for similar securities. Management determines the appropriate classification of its marketable securities at the time of purchase and reevaluates such designation

as of each balance sheet date. Short-term marketable securities have maturities less than 365 days as of the balance sheet date. Long-term marketable securities have maturities greater than 365 days as of the balance sheet date. Unrealized gains and losses are excluded from earnings and are reported as a component of comprehensive loss. Realized gains and losses and declines in fair value judged to be other than temporary, if any, on available-for-sale securities are included in interest income. The cost of securities sold is based on the specific-identification method. Interest on marketable securities is included in interest income.

Fair Value of Financial Instruments

Fair value accounting is applied for all financial assets and liabilities that are recognized or disclosed at fair value in the consolidated financial statements on a recurring basis (at least annually). The carrying amount of the Company's financial instruments, including cash equivalents, accounts payable and accrued expenses and other payables approximate fair value due to their short term maturities. See Note 3. Fair Value Measurements regarding the fair value of the Company's other financial assets and liabilities.

Property and Equipment

Property and equipment are stated at cost, net of accumulated depreciation. Depreciation is computed using the straight-line method over the estimated useful lives of the assets, ranging from three to five years. Leasehold improvements are amortized over the shorter of the lease term or the estimated useful lives of the assets. Maintenance and repairs are charged to expense as incurred. When assets are retired or otherwise disposed of, the cost and accumulated depreciation are removed from the consolidated balance sheet and any resulting gain or loss is reflected in operations in the period realized.

Impairment of Long-Lived Assets

The Company reviews long-lived assets, primarily comprised of property and equipment, for impairment or whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. Recoverability is measured by comparison of the carrying amount to the future net cash flows which the assets are expected to generate. If such assets are considered to be impaired, the impairment to be recognized is measured as the amount by which the carrying amount of the assets exceeds the projected discounted future net cash flows arising from the asset. There have been no such impairments of long-lived assets for any of the periods presented.

Accrued Research and Development Costs

The Company accrues for estimated costs of research and development activities conducted by third-party service providers, which include the conduct of preclinical studies and clinical trials, and contract manufacturing activities. The Company records the estimated costs of research and development activities based upon the estimated amount of services provided but not yet invoiced, and include these costs in accrued expenses and other payables in the consolidated balance sheets and within research and development expense in the consolidated statements of operations. These costs are a significant component of the Company's research and development expenses. The Company accrues for these costs based on factors such as estimates of the work completed and in accordance with agreements established with its third-party service providers. The Company makes significant judgments and estimates in determining the accrued liabilities balance in each reporting period. As actual costs become known, the Company adjusts its accrued liabilities. The Company has not experienced any material differences between accrued costs and actual costs incurred. However, the status and timing of actual services performed, number of patients enrolled, and the rate of patient enrollments may vary from the Company's estimates, resulting in adjustments to expense in future periods. Changes in these estimates that result in material changes to the Company's accruals could materially affect the Company's results of operations.

Comprehensive Loss

Comprehensive loss represents all changes in stockholders' equity (deficit) except those resulting from and distributions to stockholders. The Company's foreign currency translation and unrealized gains and losses on available-for-sale securities represent the only components of other comprehensive loss that are excluded from the reported net loss and that are presented in the consolidated statements of comprehensive loss.

Income Taxes

The Company uses the asset and liability method to account for income taxes in accordance with the authoritative guidance for income taxes. Under this method, deferred tax assets and liabilities are determined based on future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases, and tax loss and credit carryforwards. Deferred tax assets and liabilities are measured using enacted tax rates applied to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in income in the period that includes the enactment date. A valuation allowance is established when necessary to reduce deferred tax assets to the amount expected to be realized.

The Company recognizes the effect of income tax positions only if those positions are more likely than not of being sustained. Recognized income tax positions are measured at the largest amount that is greater than 50% likely of being realized. Changes in recognition or measurement are reflected in the period in which the change in judgment occurs. The Company records interest and penalties related to unrecognized tax benefits in income tax expense. To date, there have been no interest or penalties recorded in relation to the unrecognized tax benefits.

Research and Development Costs

Research and development costs are expensed as incurred and consist of salaries and benefits, stock-based compensation expense, lab supplies and facility costs, as well as fees paid to others that conduct certain research and development activities on the Company's behalf.

Research and Development Tax Incentive

The Company is eligible under the AusIndustry research and development tax incentive program to obtain a cash amount from the Australian Taxation Office ("ATO"). The tax incentive is available to the Company on the basis of specific criteria with which the Company must comply. Specifically, the Company must have revenue of less than AUD 20.0 million and cannot be controlled by income tax exempt entities. These research and development tax incentives are recognized as contra research and development expense when the right to receive has been attained and funds are considered to be collectible. The tax incentive is denominated in Australian dollars and, therefore, the related receivable is remeasured into U.S. dollars as of each reporting date.

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

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

SBIR Grants

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

Redeemable Convertible Preferred Stock Tranche Liability

The Company has determined that the Company's obligation to issue additional shares of the Company's redeemable convertible preferred stock represents a freestanding financial instrument, which was accounted for as a liability. The freestanding redeemable convertible preferred stock tranche liability was initially recorded at fair value, with fair value changes recognized in the consolidated statements of operations. At the time of the exercise or expiration of the option, any remaining value of the redeemable convertible preferred stock tranche liability is reclassified to redeemable convertible preferred stock with no further remeasurement required.

Redeemable Convertible Preferred Stock Warrant Liability

The Company has accounted for its freestanding warrants to purchase shares of the Company's redeemable convertible preferred stock as liabilities at fair value upon issuance. At the end of each reporting period, changes in estimated fair value during the period are recorded in the consolidated statements of operations. The Company continued to adjust the warrant liability for changes in fair value until the earlier of the exercise of the warrants or expiration on May 10, 2016, and no further remeasurement is required **.**

Stock-based Compensation

The Company measures its stock-based awards made to employees based on the estimated fair values of the awards as of the grant date using the Black-Scholes option-pricing model. Stock-based compensation expense is recognized over the requisite service period using the straight-line method and is based on the value of the portion of stock-based payment awards that is ultimately expected to vest. As such, the Company's stock-based compensation is reduced for the estimated forfeitures at the date of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates.

Stock-based compensation expense for options granted to non-employees as consideration for services received is measured on the date of performance at the fair value of the consideration received or the fair value of the equity instruments issued, using the Black-Scholes option-pricing model, whichever can be more reliably measured. Compensation expense for options granted to non-employees is periodically remeasured as the underlying options vest.

Net Loss per Share Attributable to Common Stockholders

Basic net loss per share attributable to common stockholders is calculated by dividing the net loss attributable to common stockholders by the weighted average number of shares of common stock outstanding during the period, without consideration of potentially dilutive securities. The net loss attributable to common stockholders is calculated by adjusting the net loss of the Company for the accretion on the redeemable convertible preferred stock. Diluted net loss per share attributable to common stockholders is the same as basic net loss per share attributable to common stockholders for all periods presented since the effect of potentially dilutive securities are anti-dilutive given the net loss of the Company.

Recent Accounting Pronouncements

In August 2014, the FASB issued ASU No. 2014-15, *Disclosure of Uncertainties About an Entity's Ability to Continue as a Going Concern* . ASU 2014-15 requires management to perform interim and annual assessments

of an entity's ability to continue as a going concern within one year of the date the financial statements are issued and provides guidance on determining when and how to disclose going concern uncertainties in the financial statements. Certain disclosures will be required if conditions give rise to substantial doubt about an entity's ability to continue as a going concern. ASU 2014-15 applies to all entities and is effective for annual and interim reporting periods ending after December 15, 2016, with early adoption permitted. The Company adopted this guidance effective December 31, 2016, and there was no impact on the disclosures to its consolidated financial statements.

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

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

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

In June 2016, the Financial Accounting Standards Board ("FASB") issued Accounting Standards Update ("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 ASU is effective for fiscal years and interim periods within those years beginning after December 15, 2019 and early adoption is permitted for fiscal years and interim periods within those years beginning after December 15, 2018. The Company is currently evaluating the impact of this new guidance.

In August 2016, the FASB issued ASU No. 2016-15, *Statement of Cash Flows (Topic 230) – Classification of Certain Cash Receipts and Cash Payments* , which clarifies the classification of certain cash receipts and cash

payments in the statements of cash flow to eliminate the diversity in practice related to eight specific cash flow issues. This ASU is effective for fiscal years and interim periods within those years beginning after December 15, 2017, with early adoption permitted. The Company is currently evaluating the impact of this new guidance.

In November 2016, the FASB issued ASU No. 2016-18, *Statement of Cash Flows (Topic 230) – Restricted Cash,* which requires the presentation of changes in restricted cash or restricted cash equivalents on the statement of cash flows. This ASU is effective for the fiscal years and interim periods within those years beginning after December 15, 2017, with early adoption permitted. The Company is currently evaluating the impact of this new guidance.

3. Fair Value Measurements

Financial assets and liabilities are recorded at fair value. The accounting guidance for fair value provides a framework for measuring fair value, clarifies the definition of fair value and expands disclosures regarding fair value measurements. Fair value is defined as the price that would be received to sell an asset or paid to transfer a liability (an exit price) in an orderly transaction between market participants at the reporting date. The accounting guidance establishes a three-tiered hierarchy, which prioritizes the inputs used in the valuation methodologies in measuring fair value as follows:

Level 1 —Inputs are unadjusted quoted prices in active markets for identical assets or liabilities at the measurement date.

Level 2— Inputs (other than quoted market prices included in Level 1) are either directly or indirectly observable for the asset or liability through correlation with market data at the measurement date and for the duration of the instrument's anticipated life.

Level 3 —Inputs reflect management's best estimate of what market participants would use in pricing the asset or liability at the measurement date. Consideration is given to the risk inherent in the valuation technique and the risk inherent in the inputs to the model.

In determining fair value, the Company utilizes quoted market prices, broker or dealer quotation, or valuation techniques that maximize the use of observable inputs and minimize the use of unobservable inputs to the extent possible as well as considers counterparty credit risk in its assessment of fair value.

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

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

	December 31, 2015			
	Level 1	Level 2	Level 3	Total
Assets:				
Money market funds	$2,136	$ —	$ —	$ 2,136
Corporate bonds	—	7,368	—	7,368
Commercial paper	—	500	—	500
Total financial assets	$2,136	$7,868	$ —	$10,004
Liabilities:				
Redeemable convertible preferred stock tranche liability	$ —	$ —	$1,643	$ 1,643
Redeemable convertible preferred stock warrant liability	—	—	480	480
Total financial liabilities	$ —	$ —	$2,123	$ 2,123

The corporate bonds, commercial paper and government bonds are classified as Level 2 as they were valued based upon quoted market prices for similar instruments in active markets, quoted prices for identical or similar instruments in markets that are not active and model-based valuation techniques for which all significant inputs are observable in the market or can be corroborated by observable market data for substantially the full term of the assets.

Level 3 instruments are valued based on unobservable inputs that are supported by little or no market activity and reflect the Company's assumptions in measuring fair value. The fair value measurements of the redeemable convertible preferred stock tranche liability and the redeemable convertible preferred stock warrant liability were based on significant inputs not observed in the market and thus represent a Level 3 measurement.

The redeemable convertible preferred stock tranche liability stems from the initial sale of the Company's Series C redeemable convertible preferred stock wherein the Company was obligated to sell additional shares in subsequent closings contingent upon a majority of the stockholders of the outstanding redeemable convertible preferred stock and/or the achievement of certain development milestones. The subsequent closings were deemed to be freestanding financial instruments that were at the option of the holders. The Company estimated the fair value of this liability using a one-step binomial lattice model in combination with the Option Pricing Model. The change in fair value was recognized as a gain or loss in the consolidated statements of operations. See Note 10 for further discussion on the redeemable convertible preferred stock tranche liability and related valuations.

The determination of the fair value of the redeemable convertible preferred stock warrant liability is discussed in Note 8. Generally, increases or decreases in the fair value of the underlying redeemable convertible preferred stock would result in a directionally similar impact in the fair value measurement of the warrant liability.

The following table sets forth a summary of the changes in the fair value of the Company's Level 3 financial instruments as follows (in thousands):

	Year Ended December 31,	
	2016	2015
Redeemable Convertible Preferred Stock Tranche Liability:		
Beginning balance	$ 1,643	$ —
Issuance of Series C redeemable convertible preferred stock tranche liability	—	1,017
Change in fair value upon revaluation	4,194	626
Settlement of redeemable convertible preferred stock tranche liability due to the issuance of Series C redeemable convertible preferred stock	(5,837)	—
Ending balance	$ —	$1,643

	Year Ended December 31,	
	2016	2015
Redeemable Convertible Preferred Stock Warrant Liability:		
Beginning balance	$ 480	$1,023
Change in fair value upon revaluation	525	(543)
Reclassification of redeemable convertible preferred stock warrant liability to redeemable convertible preferred stock	(1,005)	—
Ending balance	$ —	$ 480

4. Balance Sheet Components

Cash Equivalents and Available-for-sale Securities

Cash equivalents and available-for-sale securities consisted of the following (in thousands):

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

	December 31, 2015			
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
Money market funds	$ 2,136	$ —	$ —	$ 2,136
Corporate bonds	7,373	—	(5)	7,368
Commercial paper	500	—	—	500
Total cash equivalents and available-for-sale securities	$ 10,009	$ —	$ (5)	$ 10,004
Classified as:				
Cash equivalents				$ 2,136
Available-for-sale securities - current				7,868
Total cash equivalents and available-for-sale securities				$ 10,004

All available-for-sale securities - current held as of December 31, 2016 and December 31, 2015 had contractual maturities of less than one year. All available securities – noncurrent held as of December 31, 2016 had contractual maturities of greater than one year but less than two years. There have been no material realized gains or losses on available-for-sale securities for the periods presented.

Prepaid Expenses and Other Current Assets

Prepaid expenses and other current assets consisted of the following (in thousands):

	December 31,	
	2016	2015
Prepaid clinical and research related expenses	$2,488	$1,253
Other	906	305
Prepaid expenses and other current assets	$3,394	$1,558

Property and Equipment, Net

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

	December 31,	
	2016	2015
Laboratory equipment	$ 1,650	$ 1,452
Furniture and computer equipment	163	140
Leasehold improvements	62	48
Total property and equipment	1,875	1,640
Less: accumulated depreciation and amortization	(1,313)	(1,031)
Property and equipment, net	$ 562	$ 609

Depreciation expense for the years ended December 31, 2016, 2015 and 2014 was $317,000, $247,000 and $258,000, respectively. As of December 31, 2016 and 2015, $8,000 and $51,000, respectively, property and equipment, net, were located in Australia. The remainder of the assets are located in the United States.

Accrued Expenses and Other Payables

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

	December 31,	
	2016	2015
Accrued clinical and research related expenses	$3,617	$ 976
Accrued employee related expenses	1,420	754
Other	235	149
Total accrued expenses and other payables	$5,272	$1,879

5. Research Collaboration and License Agreement

In October 2013, the Company's former collaboration partner decided to abandon a collaboration program with the Company and, pursuant to the terms of the agreement between the Company and the former collaboration partner, the Company elected to assume the responsibility for the development and commercialization of the product. Upon the former collaboration partner's abandonment, it assigned to the Company certain intellectual property arising from the collaboration and also granted the Company an exclusive license to certain background intellectual property rights of the former collaboration partner that relate to the products assumed by the Company. Upon the nomination of PTG-300 as a development candidate, the Company owed the former collaboration partner a payment of $250,000. If the Company initiates a Phase 1 clinical trial for PTG-300, it will pay the former collaboration partner an additional $250,000. The Company has the right, but not the obligation, to further develop and commercialize the products and, if the Company successfully develops and

commercializes PTG-300 without a partner, the Company will pay to the former collaboration partner up to an additional aggregate of $128.5 million for the achievement of certain development, regulatory and sales milestone events. In addition, the Company will pay to the former collaboration partner a low single digit royalty on worldwide net sales of the product until the later of ten years from the first commercial sale of the product or the expiration of the last patent covering the product. For the year ended December 31, 2016, the Company recorded research and development expense of $250,000 under this agreement. There were no such costs incurred for the years ended December 31, 2015 or 2014.

6. Government Programs

Research and Development Tax Incentive

The Company recognized AUD 5.3 million ($4.0 million), AUD 978,000 ($736,000) and AUD 639,000 ($577,000) as a reduction of research and development expenses for the years ended December 31, 2016, 2015 and 2014, respectively, in connection with the research and development tax incentive from Australia. As of December 31, 2016 and December 31, 2015, the research and development tax incentive receivable was AUD 3.1 million ($2.2 million) and AUD 978,000 ($715,000), respectively.

In March 2016, the Company received AUD 237,000 ($182,000) for overseas findings and recorded the funds as deferred tax incentive in accrued expenses and other payables on the consolidated balance sheet due to the possibility that the funds could have to be repaid. In October 2016, the Company received AUD 3.0 million ($2.2 million) including interest, in connection with the Australian research and development tax incentive. Of the funds received, AUD 1.0 million ($0.7 million) reduced the research and development tax incentive receivable and AUD 2.0 million ($1.5 million), which was for overseas findings, was recorded as deferred tax incentive in accrued expenses and other payables on the consolidated balance sheet due to the risk of clawback.

In December 2016, the Company's research and development project under the AusIndustry research and development tax incentive program was complete and the Company substantiated that more than 50% of the total project expenditures occurred in Australia. Therefore, the overseas finding related incentive amounts are not deemed to be at risk of clawback and the Company recognized AUD 2.2 million ($1.6 million) as a reduction of research and development expenses for the overseas findings received in 2016.

SBIR Grant

In September 2015, the Company was awarded a Phase 1 SBIR Grant from the National Institute of Diabetes and Digestive and Kidney Diseases of the National Institutes of Health ("NIH") in support of research on orally stable peptide antagonists of the Interleukin-23 receptor ("IL-23R") as potential treatments for inflammatory bowel diseases ("IBD"). The total grant award was $224,000 and is for the period from September 2015 to August 2016.

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

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

7. Commitments and Contingencies

Lease Arrangements

The Company leases its facility under a noncancelable operating lease that expires in April 2018. The Company has provided a security deposit of $30,000 as collateral for the lease, which is included in other assets on the consolidated balance sheets.

The following table summarizes the Company's future minimum lease payments as of December 31, 2016 (in thousands):

Year Ending December 31:	Amount
2017	$ 368
2018	87
Total	$ 455

The Company's rent expense was $408,000, $280,000 and $184,000 for the years ended December 31, 2016, 2015 and 2014, respectively. Rent expense is recognized on a straight-line basis over the term of the leases and accordingly, the Company records the difference between cash rent payments and the recognition of rent expense as a deferred rent liability.

Indemnifications

In the ordinary course of business, the Company enters into agreements that may include indemnification provisions. Pursuant to such agreements, the Company may indemnify, hold harmless and defend an indemnified party for losses suffered or incurred by the indemnified party. Some of the provisions will limit losses to those arising from third party actions. In some cases, the indemnification will continue after the termination of the agreement. The maximum potential amount of future payments the Company could be required to make under these provisions is not determinable. The Company has also entered into indemnification agreements with its directors and officers that may require the Company to indemnify its directors and officers against liabilities that may arise by reason of their status or service as directors or officers to the fullest extent permitted by California corporate law. The Company currently has directors' and officers' insurance. To date, the Company has not incurred material costs to defend lawsuits or settle claims related to the indemnification agreements. The Company believes that the fair value of these indemnification agreements is minimal and has not accrued any amounts for the obligations.

8. Preferred Stock Warrants

In connection with the Series B redeemable convertible preferred stock financing, the Company issued warrants to purchase 4,000,000 shares of Series B redeemable convertible preferred stock at an exercise price of $0.01 per share. These warrants would become exercisable only when certain milestones were met on programs begun as a result of collaborations entered into in 2011 and 2012. In particular, 50% of the warrants would become exercisable upon the Company publicly announcing its first Investigational New Drug ("IND") candidate to the extent such IND candidate was the result of, or related to, the Company's previous collaboration(s) with Ironwood Pharmaceuticals and/or Zealand Pharma A/S, and the balance would become exercisable upon the first dosing of a human patient in a clinical trial that was the result of, or related to, the Company's previous collaboration(s) with Ironwood Pharmaceuticals and/or Zealand Pharma A/S. In August 2013, the initial closing date for the Series B financing, the Company issued 2,000,000 of the warrants ("First Tranche Warrants"). On August 15, 2014, in connection with the closing of the Series B second tranche financing, the Company issued the balance of the warrants ("Second Tranche Warrants").

The fair value of the warrants outstanding as of December 31, 2015 was remeasured at $480,000, determined using a one-step binomial lattice model in combination with the Option Pricing Model and the

following assumptions: risk-free interest rate of 0.90%, expected life of 1.6 years and expected volatility of 57.0% and probability of exercisability of 95% and 0% for the first tranche and second tranche, respectively.

In March 2016, the Company made a public announcement related to a preclinical candidate which triggered the achievement of the milestone and warrants to purchase 2,000,000 shares of Series B redeemable convertible preferred stock became exercisable as of that date. In April 2016, 1,999,998 shares of Series B redeemable convertible preferred stock were issued for cash proceeds of $20,000 in connection with the exercise of warrants. Immediately prior to the exercise of the warrants, the fair value of the warrants was remeasured at $1.0 million, determined using a hybrid method of the Option Pricing Model with a 67% weighted value per share and the probability-weighted expected return method ("PWERM") with a 33% weighted value per share. The following assumptions were used in the Option Pricing Model: risk-free interest rate of 0.73%, expected life of 2.0 years and expected volatility of 52.0%. The PWERM method included probabilities of three IPO scenarios occurring in July 2016. The scenarios were weighted based on the Company's estimate of each event occurring in deriving the estimated fair value. Upon the exercise of warrants, the redeemable convertible preferred stock warrant liability of $1.0 million was reclassified to redeemable convertible preferred stock.

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

The Company recorded a charge of $525,000 and $872,000 for the years ended December 31, 2016 and 2014, respectively, representing the increase in the fair value of the redeemable convertible preferred stock warrant liability in the consolidated statements of operations. The Company recorded a gain of $543,000 for the year ended December 31, 2015, representing the decrease in the fair value of the redeemable convertible preferred stock warrant liability in the consolidated statements of operations.

9. Redeemable Convertible Preferred Stock

In April 2016, 1,999,998 shares of Series B redeemable convertible preferred stock were issued in connection with the exercise of warrants for cash proceeds of $20,000.

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

The table below provides information on the Company's redeemable convertible preferred stock as of December 31, 2015 (in thousands, except shares and original issue price):

	Original Issue Price	Shares		Carrying Value	Aggregate Liquidation Preference
		Authorized	Issued and Outstanding		
Series A	$ 1.00	6,037,500	6,037,500	$ 1,751	$ 6,038
Series B	$ 0.50	40,000,000	36,000,000	18,825	18,000
Series C	$ 0.4979	80,337,411	35,147,617	16,420	17,500
Total redeemable convertible preferred stock		126,374,911	77,185,117	$ 36,996	$ 41,538

As only the passage of time was required for Series A, B and C to become redeemable, the Company was accreting the carrying value of Series A, B and C to their redemption value over the period from the respective date of issuance to July 2022, (the earliest redemption date) up to the IPO date. In the event of a change of control of the Company, proceeds would be distributed in accordance with the liquidation preferences set forth in the Company's Amended and Restated Certificate of Incorporation unless the holders of redeemable convertible

preferred stock had converted their redeemable convertible preferred stock into shares of common stock. Therefore, redeemable convertible preferred stock was classified outside of stockholders' equity (deficit) on the consolidated balance sheets, as Series A, B and C redeemable convertible preferred stock can be redeemed and as events triggering the liquidation preferences were not solely within the Company's control.

The Company recorded $558,000, $75,000, and $146,000 for the accretion of the redeemable convertible preferred stock during the years ended December 31, 2016, 2015, and 2014, respectively. The accretion was recorded as an offset to the additional paid in capital until such balance was depleted and any remaining accretion was recorded to accumulated deficit.

10. Redeemable Convertible Preferred Stock Tranche Liability

In August 2014, the Company completed the closing of the Series B Second Tranche and issued 18,000,000 shares of Series B redeemable convertible preferred stock for gross cash proceeds of $9.0 million. At this time the Series B redeemable convertible preferred stock liability was remeasured at $2.3 million using a one-step binomial lattice model in combination with option pricing method based on the following assumptions: 100% probability of achievement of the development milestones, stock price of $0.50 per share, expected term of 0 years and risk-free rate of 0.5%. Upon the closing of the Series B Second Tranche, the Series B redeemable convertible preferred stock liability was terminated and the balance of the liability of $2.3 million was reclassified to redeemable convertible preferred stock.

In July 2015, the Company entered into the Series C Preferred Stock Purchase Agreement ("the Series C Agreement") for the issuance of up to 80,337,411 shares of Series C redeemable convertible preferred stock at a price of $0.4979 per share, in multiple closings. The initial closing occurred on July 10, 2015, whereby 35,147,617 shares of Series C redeemable convertible preferred stock were issued for gross proceeds of approximately $17.5 million. According to the initial terms of the Series C Agreement, the Company could issue 45,189,794 additional shares under the same terms as the initial closing, in a subsequent closing ("Series C Second Tranche") contingent upon the achievement of certain development milestones.

On the date of the initial closing, the Company recorded a Series C redeemable convertible preferred stock liability of $1.0 million, as the fair value of the obligation/right to complete the Series C Second Tranche. The fair value of the Series C redeemable convertible preferred stock liability on the date of the initial closing was determined using a one-step binomial lattice model in combination with the option pricing method based on the following assumptions: 90% probability of achievement of the development milestones, stock price of $0.4979 per share, expected term of 1.0 year, and risk-free rate of 0.5%.

At December 31, 2015, the fair value of the Series C redeemable convertible preferred stock liability was remeasured and determined to be $1.6 million using a one-step binomial lattice model in combination with the Option Pricing Model based on the following assumptions: 95% probability of achievement of the development milestones, stock price of $0.4979 per share, expected term of 0.53 year, and risk-free rate of 0.9%.

In March 2016, the Company completed the closing of the Series C Second Tranche and issued 45,189,794 shares of Series C redeemable convertible preferred stock for net cash proceeds of $22.5 million. At this time the Series C redeemable convertible preferred stock liability was remeasured at $5.8 million, determined using a hybrid method of the Option Pricing Model with a 67% weighted value per share and the PWERM with a 33% weighted value per share. The following assumptions were used in the Option Pricing Model: risk-free interest rate of 0.73%, expected life of 2.0 years and expected volatility of 52.0%. The PWERM method included probabilities of three IPO scenarios occurring in July 2016. The scenarios were weighted based on the Company's estimate of each event occurring in deriving the estimated fair value. Upon the closing of the Series C Second Tranche, the Series C redeemable convertible preferred stock liability was terminated and the balance of the liability of $5.8 million was reclassified to redeemable convertible preferred stock.

For the years ended December 31, 2016, 2015 and 2014, the Company recorded a charge of $4.2 million, $626,000 and $897,000, respectively, for the change in the fair value of the redeemable convertible preferred stock liability in the consolidated statements of operations.

11. Common Stock

The Company had reserved shares of common stock for issuance, on an as-converted basis, as follows:

	December 31,	
	2016	2015
Redeemable convertible preferred stock outstanding	—	5,323,103
Options issued and outstanding	2,393,829	833,178
Options available for future grants	164,328	147,219
Redeemable convertible preferred stock warrants	—	275,861
Total	2,558,157	6,579,361

12. Equity Plans

Equity Incentive Plan

In May 2007, the Company established its 2007 Stock Option and Incentive Plan (the "2007 Plan") which provides for the granting of stock options to employees and consultants of the Company. Options granted under the 2007 Plan may be either incentive stock options (ISOs) or nonqualified stock options (NSOs). ISOs may be granted only to Company employees (including officers and directors who are also employees). NSOs may be granted to Company employees and consultants. 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 (the "2016 Plan") to replace the 2007 Stock Option Plan and became effective upon the IPO. 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. Under the 2016 Plan, 1,200,000 shares of the Company's common stock have been initially reserved for the issuance of stock options, restricted stock units and other awards to employees, directors and consultants. Options granted under the 2016 Plan expire no later than 10 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. Upon adoption of the 2016 Plan, no additional stock awards will be issued under the 2007 Stock Option Plan. Options granted under the 2007 Stock Option Plan that were outstanding on the date the 2016 plan became effective remain subject to the terms of the 2007 Stock Option 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, 2016, the Company has reserved 1,200,000 shares of common stock for issuance under the 2016 Plan.

Stock Options

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

	Options Available for Grant	Options Outstanding	Options Outstanding: Weighted-Average Exercise Price Per Share	Options Outstanding: Weighted-Average Remaining Contractual Life (years)	Options Outstanding: Aggregate Intrinsic Value (in thousands)
Balances at December 31, 2013	70,082	284,879	$ 1.10	7.92	
Additional options authorized	240,425	—			
Options granted	(199,519)	199,519	1.83		
Options exercised	—	(2,548)	1.30		
Options forfeited	5,844	(5,844)	1.13		
Balances at December 31, 2014	116,832	476,006	1.40	8.04	
Additional options authorized	431,411	—			
Options granted	(408,623)	408,623	1.24		
Options exercised	—	(43,852)	1.30		
Options forfeited	7,599	(7,599)	1.40		
Balances at December 31, 2015	147,219	833,178	1.33	8.56	
Additional options authorized	1,697,088	—			
Options granted	(1,679,979)	1,679,979	14.24		
Options exercised	—	(119,328)	1.28		
Balances at December 31, 2016	164,328	2,393,829	$ 10.39	8.79	$ 27,820
Options exercisable – December 31, 2016		492,714	$ 5.19	7.70	$ 8,286
Options vested and expected to vest – December 31, 2016		2,369,135	$ 10.37	8.79	$ 27,596

The aggregate intrinsic values of options outstanding, exercisable, vested and expected to vest were calculated as the difference between the exercise price of the options and the fair value of the Company's common stock on December 31, 2016. The aggregate intrinsic value of options exercised was $169,000 for the year ended December 31, 2016. The aggregate intrinsic value of options exercised was immaterial for the years ended December 31, 2015 and 2014, respectively.

During the years ended December 31, 2016, 2015, and 2014 the estimated weighted-average grant-date fair value of common stock underlying options granted was $8.20, $0.69, and $0.82 per share, respectively.

Employee Stock Options Valuation

The fair value of employee and director stock option awards was estimated at the date of grant using a Black-Scholes option-pricing model with the following assumptions:

	Year Ended December 31,		
	2016	2015	2014
Expected term (in years)	4.16 – 5.95	5.89	6.08
Expected volatility	62.5 – 64.8%	59.8%	64.7%
Risk-free interest rate	1.27 – 1.79%	1.57 – 1.58%	1.89%
Dividend yield	—	—	—

Prior to the completion of the Company's IPO, the fair value of the Company's shares of common stock underlying its stock options had historically been determined by the Company's Board of Directors. Because

there had been no public market for the Company's common stock prior to August 2016, the Company's Board of Directors had determined fair value of the common stock at the time of grant of the option by considering a number of objective and subjective factors including important developments in the Company's operations, valuations performed by an independent third party, sales of redeemable convertible preferred stock, actual operating results and financial performance, the conditions in the biotechnology industry and the economy in general, the stock price performance and volatility of comparable public companies, and the lack of liquidity of the Company's common stock, among other factors. For stock options granted after the completion of the IPO, the Company's Board of Directors determined the fair value of each share of underlying common stock based on the closing price of the Company's common stock as reported on the date of grant.

In determining the fair value of the options granted, the Company uses the Black-Scholes option-pricing model and assumptions discussed below. Each of these inputs is subjective and generally requires significant judgment to determine.

Expected Term —The Company's expected term represents the period that the Company's options granted are expected to be outstanding and is determined using the simplified method (based on the mid-point between the vesting date and the end of the contractual term). The Company has very limited historical information to develop reasonable expectations about future exercise patterns and post-vesting employment termination behavior for its stock option grants.

Expected Volatility —Since the Company does not have a long trading history for its common stock, the expected volatility is estimated based on the average volatility for comparable publicly traded biopharmaceutical companies over a period equal to the expected term of the stock option grants. The comparable companies were chosen based on their similar size, stage in the life cycle or area of specialty.

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

Expected Dividend —The Company has never paid dividends on its common stock and has no plans to pay dividends on its common stock. Therefore, the Company used an expected dividend yield of zero.

Stock Options Granted to Non-employees

Stock-based compensation related to stock options granted to non-employees is recognized as the stock options are earned. The fair value of the stock options granted was calculated at each reporting date using the Black-Scholes option-pricing model with the following assumptions:

	Year Ended December 31,		
	2016	2015	2014
Expected term (in years)	6.59 – 9.97	6.8	9.4
Expected volatility	62.5 – 62.8%	59.8%	64.7%
Risk-free interest rate	1.29 – 1.79%	1.95%	2.34%
Dividend yield	—	—	—

During the years ended December 31, 2016, 2015, and 2014 the Company granted 59,647, 4,816, and 11,805 shares, respectively, to non-employee consultants. The Company recorded stock-based compensation expense during the years ended December 31, 2016, 2015, and 2014 of $505,000, $15,000, and $5,000, respectively.

Employee Stock Purchase Plan

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

as an employee stock purchase plan under Section 423 of the Internal Revenue Code of 1986, as amended, and is administered by the Company's board of directors and the Compensation Committee of the board of directors. Under the 2016 ESPP, 150,000 shares of the Company's common stock have been initially reserved for employee purchases of the Company's common stock, with an automatic annual increase to the shares issuable under the 2016 ESPP on the first day of each fiscal year for a period of up to 10 years in an amount equal to (i) the lesser of 1% of the total number of shares of common stock outstanding on December 31 of the preceding fiscal year and 300,000 shares of the Company's common stock, or (ii) a lower number 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, 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.

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, 2016
Expected term (in years)	0.60
Expected volatility	52.48%
Risk-free interest rate	0.45%
Dividend yield	—

Stock-Based Compensation

Total stock-based compensation expense recognized for both employees and non-employees for stock options and the 2016 ESPP was as follows (in thousands):

	Year Ended December 31,		
	2016	2015	2014
Research and development	$ 1,080	$ 39	$ 17
General and administrative	1,050	60	25
Total stock-based compensation expense	$ 2,130	$ 99	$ 42

As of December 31, 2016 there was $12.6 million of total unrecognized stock-based compensation costs related to stock options that the Company expects to recognize over a period of approximately 3.12 years.

13. 401(k) Plan

In March 2012, the Company adopted a retirement and savings plan under Section of 401(k) of Internal Revenue Code (the 401(k) Plan) covering all employees. The 401(k) Plan allows employees to make pre- and post-tax contributions up to the maximum allowable amount set by the IRS. The Company does not make matching contributions to the 401(k) plan on behalf of participants.

14. Income Taxes

No provision for income taxes was recorded for the years ended December 31, 2016, 2015 and 2014. The Company has incurred net operating losses for all the periods presented. The Company has not reflected any benefit of such net operating loss carryforwards in the consolidated financial statements. The Company has established a full valuation allowance against its deferred tax assets due to the uncertainty surrounding the realization of such assets.

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

	Year Ended December 31,		
	2016	2015	2014
Domestic	$(34,977)	$(10,483)	$ (9,515)
Foreign	(2,200)	(4,375)	(1,557)
Total net loss	$(37,177)	$(14,858)	$(11,072)

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

	Year Ended December 31,		
	2016	2015	2014
Federal statutory income tax rate	34.0%	34.0%	34.0%
State taxes, net of federal benefit	6.5	(2.7)	4.1
Warrant revaluation	(4.3)	(0.2)	(5.5)
Foreign tax rate difference	(1.6)	(11.8)	(6.8)
Change in valuation allowance	(36.0)	(19.9)	(26.5)
Other	1.4	0.6	0.7
Provision for income taxes	0.0%	0.0%	0.0%

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

	December 31,	
	2016	2015
Deferred tax assets:		
Net operating loss carryforwards	$ 21,501	$ 9,513
Depreciation and amortization	419	480
Accruals/other	908	293
Research and development credits & foreign credits	1,143	285
Total deferred tax assets	23,971	10,571
Valuation allowance	(23,971)	(10,571)
Net deferred tax assets	$ —	$ —

Realization of the deferred tax assets is dependent upon future taxable income, if any, the amount and timing of which are uncertain. The Company has established a valuation allowance to offset deferred tax assets as of December 31, 2016 and 2015 due to the uncertainty of realizing future tax benefits from its net operating loss carryforwards and other deferred tax assets. The valuation allowance increased by approximately $13.4 million, $3.0 million and $2.9 million during the year ended December 31, 2016, 2015 and 2014, respectively. The increase in the valuation allowance is mainly related to the increase in net operating loss carryforwards incurred during the respective taxable years.

At December 31, 2016, the Company had net operating loss carryforwards for federal income tax purposes of approximately $48.0 million which are available to offset future taxable income, if any, through 2033 and net operating loss carryforwards for state income tax purposes of approximately $37.7 million which are available to offset future taxable income, if any, through 2033.

At December 31, 2016 the Company also had accumulated Australian tax losses of $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. As of December 31, 2016, the Company also had $1.1 million of federal and $0.6

million of state research and development tax credit carryforwards available to reduce future income taxes. The federal research and development tax credits will begin to expire in 2035, if not utilized. The state research and development tax credits have no expiration date.

Federal and state laws impose substantial restrictions on the utilization of net operating loss and tax credit carryforwards in the event of an ownership change for tax purposes, as defined in Section 382 of the Internal Revenue Code. As a result of such ownership changes, the Company's ability to realize the potential future benefit of tax losses and tax credits that existed at the time of the ownership change may be significantly reduced. The Company's deferred tax asset and related valuation allowance would be reduced as a result.

It is the Company's policy to include penalties and interest expense related to income taxes as a component of other expense, as necessary.

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

	Year Ended December 31,		
	2016	2015	2014
Balance at beginning of year	$ 805	$ —	$ —
Additions based on tax positions related to in prior years	707	690	—
Additions based on tax positions related to current year	619	115	—
Balance at end of year	$ 2,131	$ 805	$ —

The Company does not expect that its uncertain tax positions will materially change in the next twelve months. The reversal of the uncertain tax benefits would not impact the Company's effective tax rate as the Company continues to maintain a full valuation allowance against its deferred tax assets.

The Company files income tax returns in the United States federal jurisdiction, the State of California and Australia. The Company is not currently under examination by income tax authorities in federal, state or other jurisdictions. The Company's tax returns for 2012 through 2016 remain open for examination due to the carryover of unused net operating losses and tax credits.

15. Net Loss per Share Attributable to Common Stockholders

As the Company had net losses for the years ended December 31, 2016, 2015 and 2014, all potential common shares were determined to be anti-dilutive. The following table sets forth the computation of the basic and diluted net loss per share attributable to common stockholders (in thousands, except share and per share data):

	Year Ended December 31,		
	2016	2015	2014
Numerator:			
Net loss	$ (37,177)	$ (14,858)	$ (11,072)
Accretion of redeemable convertible preferred stock	(558)	(75)	(146)
Net loss attributable to common stockholders	$ (37,735)	$ (14,933)	$ (11,218)
Denominator:			
Weighted-average shares used to compute net loss per common share, basic and diluted	6,501,796	251,717	227,197
Net loss per share attributable to common stockholders, basic and diluted	$ (5.80)	$ (59.32)	$ (49.38)

The following outstanding shares of potentially dilutive securities have been excluded from diluted net loss per share calculations for the years ended December 31, 2016, 2015 and 2014, because their inclusion would be anti-dilutive:

	Year Ended December 31,		
	2016	2015	2014
Redeemable convertible preferred stock on an as-converted basis	—	5,323,103	2,899,134
Options to purchase common stock	2,393,829	833,178	476,006
Warrants to purchase redeemable convertible preferred stock on an as-converted basis	—	275,861	275,861
Total	2,393,829	6,432,142	3,651,001

16. Subsequent Events

In March 2017, the Company entered into a lease agreement for a new office and laboratory space in Newark, California to relocate its operations to a larger facility. The lease commencement date is July 1, 2017 and the lease expires on June 30, 2024. The Company aggregate minimum lease payments totaling $13.4 million under the lease agreement and will provide the landlord with a letter of credit as the security deposit of $450,000.

17. Supplementary Financial Data (unaudited)

The following table presents the selected quarterly financial data for the years ended December 31, 2016 and 2015:

	Consolidated Statements of Operations			
	Quarter Ended			
	March 31	June 30	September 30	December 31
	(In thousands, except per share amounts)			
2016				
Loss from operations	$ (7,040)	$(7,091)	$ (7,138)	$ (11,397)
Net loss	$(11,747)	$(7,098)	$ (7,084)	$ (11,248)
Net loss per share of common stock attributable to common stockholders, basic and diluted	$ (40.96)	$(19.07)	$ (0.87)	$ (0.67)
2015				
Loss from operations	$ (2,689)	$(3,083)	$ (4,021)	$ (5,001)
Net loss	$ (2,697)	$(3,219)	$ (3,449)	$ (5,493)
Net loss per share of common stock attributable to common stockholders, basic and diluted	$ (11.75)	$(13.78)	$ (12.79)	$ (20.31)

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

None.

Item 9A. Controls and Procedures

Evaluation of disclosure controls and procedures

Management, under the supervision and with the participation of our Chief Executive Officer and Chief Financial Officer, have 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, 2016. 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 were not effective as of December 31, 2016 to provide reasonable assurance because of the material weaknesses in our internal controls over financial reporting as described below.

Exemption from management's report on internal control over financial reporting for the fiscal year ended December 31, 2016

This Annual Report on Form 10-K does not include a report of management's assessment regarding internal control over financial reporting on an attestation report of our independent registered public accounting firm due to a transition period established by the rules of the Securities and Exchange Commission for newly public companies.

Material Weaknesses

In connection with the audit of our consolidated financial statements for the years ended December 31, 2015 and 2014, we and our independent registered public accounting firm identified two material weaknesses in our internal control over financial reporting. A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting such that there is a reasonable possibility that a material misstatement of our annual or interim financial statements will not be prevented or detected on a timely basis.

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

Remediation Plans

While we intend to implement a plan to remediate the material weaknesses, we have not completed the implementation of this plan as of December 31, 2016. Accordingly, we continue to have the material weaknesses as of December 31, 2016. We can give no assurance that our current and planned implementation will remediate this deficiency in internal control or that additional material weaknesses or significant deficiencies in our internal control over financial reporting will not be identified in the future. Our plan to remediate the material weaknesses includes implementing a new accounting software system, adding additional accounting personnel and performing a review of manual journal entries. We identified and began implementation of an accounting system to improve our information systems related controls, which went into production in early 2017. We have recruited and intend to continue to recruit additional finance and accounting personnel as needed to enhance segregation of duties, we will continue to utilize consultants with technical accounting expertise as needed, and we will establish formal written policies for our accounting function.

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

Entry into a Material Definitive Agreement.

On March 6, 2017, we entered into a Lease (the " ***Lease*** ") with BMR-Pacific Research Center LP of approximately 42,877 rentable square feet of office and laboratory space located at 7707 Gateway Boulevard, Newark, California (the " ***Facility*** ").

The term of the Lease commences when we commence business operations in the Facility, but in no event earlier than June 1, 2017 or later than July 1, 2017. Upon commencement of the Lease, the Lease has a term of seven years. The monthly base rent starts at $3.40 per square foot in the first year of the Lease, increases to $3.60 per square foot in the second year of the Lease, and escalates by 3.0% annually each year thereafter.

The foregoing description of the Lease does not purport to be complete and is qualified in its entirety by reference to the Lease, a copy of which is filed as Exhibit 10.9 to this annual report on Form 10-K and is incorporated herein by reference.

PART III

Item 10. Directors, Executive Officers, 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 2017 Annual Meeting of Stockholders within 120 days after the end of the fiscal year ended December 31, 2016.

We have adopted a Code of Business Conduct and Ethics that applies to all of our directors, officers and employees, including our principal executive officer and principal financial officer. The Code of Business Conduct and Ethics is posted on our website at http://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 2017 Annual Meeting of Stockholders within 120 days after the end of the fiscal year ended December 31, 2016.

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 2017 Annual Meeting of Stockholders within 120 days after the end of the fiscal year ended December 31, 2016.

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 2017 Annual Meeting of Stockholders within 120 days after the end of the fiscal year ended December 31, 2016.

Item 14. Principal Accountant 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 2017 Annual Meeting of Stockholders within 120 days after the end of the fiscal year ended December 31, 2016.

PART IV

Item 15. Exhibits and 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.

SIGNATURES

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

PROTAGONIST THERAPEUTICS, INC.

Date: March 7, 2017

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

POWER OF ATTORNEY

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

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

Signature	Title	Date
/s/ Dinesh V. Patel, Ph.D. Dinesh V. Patel, Ph.D.	President, Chief Executive Officer and Director *(Principal Executive Officer PEO)*	March 7, 2017
/s/ Thomas P. O'Neil Thomas P. O'Neil	Chief Financial Officer *(Principal Financial and Accounting Officer PFO and AO)*	March 7, 2017
/s/ Harold E. Selick, Ph.D Harold E. Selick, Ph.D	Chairman of the Board of Directors	March 7, 2017
/s/ Chaitan Khosla, Ph.D. Chaitan Khosla, Ph.D.	Director	March 7, 2017
/s/ Julie Papanek Julie Papanek	Director	March 7, 2017
/s/ Armen Shanafelt, Ph.D. Armen Shanafelt, Ph.D.	Director	March 7, 2017
/s/ William D. Waddill William D. Waddill	Director	March 7, 2017

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	001-3785237852	3.1	08/16/2016	
3.2	Amended and Restated Bylaws	S-1/A	333-212476	3.2	08/01/2016	
4.1	Specimen stock certificate evidencing the shares of common stock	S-1/A	333-212476	4.1	08/01/2016	
4.2	Amended and Restated Investor Rights Agreement, by and among Protagonist Therapeutics, Inc. and the stockholders named therein, dated July 10, 2015.	S-1/A	333-212476	4.2	08/01/2016	
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	07/11/2016	
10.2+	Protagonist Therapeutics, Inc. 2016 Equity Incentive Plan and forms of stock option grant notice, option agreement, notice of exercise, restricted stock unit grant notice and restricted stock unit agreement thereunder.	S-1/A	333-212476	10.2	08/01/2016	
10.3+	Protagonist Therapeutics, Inc. 2016 Employee Stock Purchase Plan.	S-1/A	333-212476	10.3	08/01/2016	
10.4+	Form of Indemnity Agreement for Directors and Officers.	S-1/A	333-212476	10.4	08/01/2016	
10.5	Lease, dated September 30, 2013, by and between the Registrant and Berrueta Family Partnership.	S-1	333-212476	10.5	07/11/2016	
10.6	First Amendment to Lease, dated March 24, 2014, by and between the Registrant and Berrueta Family Partnership.	S-1	333-212476	10.6	07/11/2016	
10.7	Second Amendment to Lease, dated May 4 2015, by and between the Registrant and Berrueta Family L.P.	S-1	333-212476	10.7	07/11/2016	
10.8	Third Amendment to Lease, dated August 11, 2015, by and between the Registrant and Berrueta Family L.P.	S-1	333-212476	10.8	07/11/2016	
10.9	Lease, dated March 6, 2017, by and between the Registrant and BMR-Pacific Research Center LP.					X

Exhibit Number	Exhibit Description	Incorporation By Reference				Filed Herewith
		Form	SEC File No.	Exhibit	Filing Date	
10.10+	Severance Agreement, dated August 1, 2016, by and between the Registrant and Dinesh Patel.	S-1/A	333-212476	10.9	08/01/2016	
10.11+	Severance Agreement, dated August 1, 2016, by and between the Registrant and David Y. Liu, Ph.D.	S-1/A	333-212476	10.10	08/01/2016	
10.12+	Severance Agreement, dated August 1, 2016, by and between the Registrant and William Hodder.	S-1/A	333-212476	10.11	08/01/2016	
10.13+	Severance Agreement, dated August 1, 2016, by and between the Registrant and Tom O'Neil.	S-1/A	333-212476	10.12	08/01/2016	
10.14+	Severance Agreement, dated August 1, 2016, by and between the Registrant and Richard Shames, M.D.	S-1/A	333-212476	10.13	08/01/2016	
10.15†	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	07/11/2016	
10.16†	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	07/11/2016	
10.17†	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	07/11/2016	
10.18†	Protagonist Assumption of Responsibility, dated January 28, 2014, by and between the Registrant and Zealand Pharma A/S.	S-1	333-212476	10.20	07/11/2016	
10.19†	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	07/11/2016	
10.20†	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	07/11/2016	
10.21	Letter Agreement, dated as of May 10, 2013, by and between the Registrant and Johnson & Johnson Development Corporation, as amended.	S-1	333-212476	10.23	07/11/2016	

Exhibit Number	Exhibit Description	Incorporation By Reference				Filed Herewith
		Form	SEC File No.	Exhibit	Filing Date	
21.1	List of Subsidiaries					X
23.1	Consent of Independent Registered Public Accounting Firm					X
24.1	Power of Attorney (included in signature page of this Form 10-K)					X
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.

Exhibit 10.9

LEASE

by and between

BMR-PACIFIC RESEARCH CENTER LP,
a Delaware limited partnership

and

PROTAGONIST THERAPEUTICS, INC.,
a Delaware corporation

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LEASE

THIS LEASE (this " Lease ") is entered into as of this 6th day of March, 2017 (the " Execution Date "), by and between BMR-PACIFIC RESEARCH CENTER LP, a Delaware limited partnership (" Landlord "), and PROTAGONIST THERAPEUTICS, INC., a Delaware corporation (" Tenant ").

RECITALS

A. WHEREAS, Landlord owns certain real property (the " Property ") and the improvements on the Property located at 7333-7999 Gateway Boulevard, Newark, California, including the buildings located thereon; and

B. WHEREAS, Landlord wishes to lease to Tenant, and Tenant desires to lease from Landlord, certain premises as shown on Exhibit A attached hereto (the " Premises ") located on the first (1 st) and second (2 nd) floors of the building addressed at 7707 Gateway Boulevard, Newark, California (the " Building "), pursuant to the terms and conditions of this Lease, as detailed below.

AGREEMENT

NOW, THEREFORE, Landlord and Tenant, in consideration of the mutual promises contained herein and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, and intending to be legally bound, agree as follows:

1. Lease of Premises

1.1. Effective on the Term Commencement Date (as defined below), Landlord hereby leases to Tenant, and Tenant hereby leases from Landlord, the Premises, including exclusive shafts, cable runs and mechanical spaces, for use by Tenant in accordance with the Permitted Use (as defined below) and no other uses. The Property and all landscaping, parking facilities, private drives and other improvements and appurtenances related thereto, including the Building, the Amenities Building (as defined below), the nine (9) other buildings currently located on the Property and each additional building that is constructed on the Property (following substantial completion of such building), are hereinafter collectively referred to as the " Project ." All portions of the Building that are for the non-exclusive use of the tenants of the Building only, and not the tenants of the Project generally, such as service corridors, stairways, elevators, public restrooms and public lobbies (all to the extent located in the Building), are hereinafter referred to as " Building Common Area ." All portions of the Project that are for the non-exclusive use of tenants of the Project generally, including driveways, sidewalks, parking areas, landscaped areas, and (to the extent not located in a building other than the Amenities Building) service corridors, stairways, elevators, public restrooms, public lobbies and the amenities building (the " Amenities Building ") in which Landlord currently provides certain amenities, including food services, a fitness center and a conference center (" Amenities Building Services ") (but excluding Building Common Area), are hereinafter referred to as " Project Common Area ." The Building Common Area and Project Common Area are collectively referred to herein as " Common Area ." The Building is located on a portion of the Project commonly referred to as the "North Campus,"

which is that part of the Project to the north of Gateway Boulevard comprised of the Building and five (5) other buildings commonly referred to as Buildings 1, 2, 3, 6 and 7, together with all appurtenances thereto (collectively, the " North Campus ").

2. Basic Lease Provisions . For convenience of the parties, certain basic provisions of this Lease are set forth herein. The provisions set forth herein are subject to the remaining terms and conditions of this Lease and are to be interpreted in light of such remaining terms and conditions.

2.1. This Lease shall take effect upon the Execution Date and, except as specifically otherwise provided within this Lease, each of the provisions hereof shall be binding upon and inure to the benefit of Landlord and Tenant from the date of execution and delivery hereof by all parties hereto.

2.2. In the definitions below, each current Rentable Area (as defined below) is expressed in square feet. Rentable Area and " Tenant's Pro Rata Shares " are all subject to adjustment as provided in this Lease.

Definition or Provision	Means the Following (As of the Term Commencement Date)
Approximate Rentable Area of Premises	42,877 square feet
Approximate Rentable Area of Building	148,848 square feet
Approximate Rentable Area of North Campus	966,271 square feet
Approximate Rentable Area of Project	1,389,517 square feet
Tenant's Pro Rata Share of Building	28.81%
Tenant's Pro Rata Share of North Campus	4.44%
Tenant's Pro Rata Share of Project	3.09%

2.3. Initial monthly installments of Base Rent for the Premises (" Base Rent ") as of the Term Commencement Date, subject to adjustment under this Lease:

Dates	Square Feet of Rentable Area	Base Rent per Square Foot of Rentable Area	Monthly Base Rent
Month 1 – Month 6	21,291*	$3.40 monthly	$ 72,389.40
Month 7 – Month 12	31,291*	$3.40 monthly	$ 106,389.40
Month 13 – Month 24	42,877	$3.60 monthly	$ 154,357.20

* *Base Rent for months one (1) through (6) of the Term will be calculated based upon 21,291 square feet of Rentable Area and Base Rent for months seven (7) through twelve (12) of the Term will be calculated based upon 31,291 square feet of Rentable Area; provided , however, that Tenant's Pro Rata Shares shall, at all times, be calculated based on the total Rentable Area of the Premises.*

2.4. Estimated Term Commencement Date: July 1, 2017

2.5. Estimated Term Expiration Date: June 30, 2024

2.6. Security Deposit: $450,000 (subject to Section 11.7 below)

2.7. Permitted Use: Office, R&D, laboratory and vivarium use in conformity with all federal, state, municipal and local laws, codes, ordinances, rules and regulations of Governmental Authorities (as defined below), committees, associations, or other regulatory committees, agencies or governing bodies having jurisdiction over the Premises, the Building, the Property, the Project, Landlord or Tenant, including both statutory and common law and hazardous waste rules and regulations (" Applicable Laws ")

2.8. Address for Rent Payment:

BMR-Pacific Research Center LP
Attention Entity 285
P.O. Box 511415
Los Angeles, California 90051-7970

2.9. Address for Notices to Landlord:

BMR-Pacific Research Center LP
17190 Bernardo Center Drive
San Diego, California 92128
Attn: Legal Department

2.10. Address for Notices to Tenant:

Protagonist Therapeutics, Inc.
7707 Gateway Boulevard,
Newark, California
Attn: Tom O'Neil, Chief Financial Officer

2.11. Address for Invoices to Tenant:

Protagonist Therapeutics, Inc.
7707 Gateway Boulevard,
Newark, California
Attn: Tom O'Neil, Chief Financial Officer

2.12. The following Exhibits are attached hereto and incorporated herein by reference:

Exhibit A	Premises
Exhibit B	Work Letter
Exhibit B-1	Tenant Work Insurance Schedule
Exhibit C	Acknowledgement of Term Commencement Date and Term Expiration Date
Exhibit D	FF&E
Exhibit E	Form of Letter of Credit
Exhibit F	Rules and Regulations
Exhibit G	Approved Vendor List
Exhibit H	Tenant's Personal Property
Exhibit I	Form of Estoppel Certificate
Exhibit J	Landlord Work Area

3. Term . The actual term of this Lease (as the same may be earlier terminated in accordance with this Lease, the " Term ") shall commence on the actual Term Commencement Date (as defined in Article 4) and end on the date (the " Term Expiration Date ") that is eighty-four (84) months after the actual Term Commencement Date, subject to earlier termination of this Lease as provided herein. TENANT HEREBY WAIVES THE REQUIREMENTS OF SECTION 1933 OF THE CALIFORNIA CIVIL CODE, AS THE SAME MAY BE AMENDED FROM TIME TO TIME.

4. Possession and Commencement Date .

4.1. The " Term Commencement Date " shall be the earlier of (a) the Estimated Term Commencement Date and (b) the later of (i) June 1, 2017 and (ii) the day Tenant commences business operations in the Premises. Tenant shall execute and deliver to Landlord written acknowledgment of the actual Term Commencement Date and the Term Expiration Date within ten (10) days after Tenant takes occupancy of the Premises, in the form attached as Exhibit C hereto. Failure to execute and deliver such acknowledgment, however, shall not affect the Term Commencement Date or Landlord's or Tenant's liability hereunder. Failure by Tenant to obtain validation by any medical review board or other similar governmental licensing of the Premises required for the Permitted Use by Tenant shall not serve to extend the Term Commencement Date. The term " Substantially Complete " or " Substantial Completion " means that the Tenant Improvements (as defined below) are substantially complete in accordance with the Approved Plans (as defined in the Work Letter), except for minor punch list items.

4.2. Tenant shall cause the work (the " Tenant Improvements ") described in the Work Letter attached hereto as Exhibit B (the " Work Letter ") to be constructed in the Premises pursuant to the Work Letter at a cost to Landlord not to exceed Four Hundred Sixty-Nine Thousand Three Hundred Sixty-Five Dollars ($469,365) (the " TI Allowance "). The TI Allowance may be applied to the costs of (m) construction, (n) project review by Landlord (which fee shall equal three percent (3%) of the cost of the Tenant Improvements, including the TI Allowance), (o) commissioning of mechanical, electrical and plumbing systems by a licensed, qualified commissioning agent hired by Tenant, and review of such party's commissioning

report by a licensed, qualified commissioning agent hired by Landlord, (p) space planning, architect, engineering and other related services performed by third parties unaffiliated with Tenant, (q) building permits and other taxes, fees, charges and levies by Governmental Authorities (as defined below) for permits or for inspections of the Tenant Improvements, and (r) costs and expenses for labor, material, equipment and fixtures. In no event shall the TI Allowance be used for (v) the cost of work that is not authorized by the Approved Plans (as defined in the Work Letter) or otherwise approved in writing by Landlord, (w) payments to Tenant or any affiliates of Tenant, (x) the purchase of any furniture, personal property or other non-building system equipment, (y) costs resulting from any default by Tenant of its obligations under this Lease or (z) costs that are recoverable by Tenant from a third party (e.g., insurers, warrantors, or tortfeasors).

4.3. Tenant shall have until December 31, 2018 to expend the unused portion of the TI Allowance, after which date Landlord's obligation to fund such costs shall expire.

4.4. In no event shall any unused TI Allowance entitle Tenant to a credit against Rent payable under this Lease. Tenant shall deliver to Landlord (a) a certificate of occupancy (or its substantial equivalent) for the Premises suitable for the Permitted Use (if required by Applicable Law for legal occupancy of the Premises) and (b) a Certificate of Substantial Completion in the form of the American Institute of Architects document G704, executed by the project architect and the general contractor.

4.5. Tenant shall have exclusive access to the Premises (subject to the terms, conditions and provisions of Section 4.6 below) from and after the Execution Date for purposes of (a) constructing the Tenant Improvements (in accordance with all of the terms, conditions and provisions of this Lease and the Work Letter), (b) the placement of Tenant's furniture, fixtures, equipment and personal property, and (c) commencing business operations in the Premises; provided , however, that, prior to entering upon the Premises, Tenant shall furnish to Landlord evidence satisfactory to Landlord that insurance coverages required of Tenant under the provisions of Article 23 are in effect, and such entry shall be subject to all the terms and conditions of this Lease other than the payment of Base Rent, the Property Management Fee (as defined below) or Tenant's Adjusted Share of Operating Expenses (as defined below) (except that, in the event that Tenant uses the Premises for the purposes set forth in Subsection (c) above prior to the Term Commencement Date, Tenant shall be obligated to pay the Property Management Fee and Tenant's Adjusted Share of Operating Expenses from and after the date that Tenant first commences business operations in the Premises).

4.6 Notwithstanding anything to the contrary in this Lease, Tenant acknowledges that, as of the Execution Date, Landlord is in the process of constructing certain work on the slab, vapor barrier and flooring in the portion of the first (1 st) floor of the Premises outlined on Exhibit J attached hereto (such work, the " Landlord Work "). From and after the Execution Date, Tenant shall permit Landlord to enter the Premises at all times (including during business hours) to construct the Landlord Work, and Tenant shall (at no cost to Tenant) otherwise reasonably cooperate with Landlord throughout the construction process to enable Landlord to complete the Landlord Work in a timely and efficient manner. In constructing the Landlord Work, Landlord shall reasonably cooperate with Tenant so as to cause as little interference to Tenant as is

reasonably possible; provided , however, that in no event shall Landlord's construction of the Landlord Work in the Premises (a) cause Rent (as defined below) to abate under this Lease, (b) give rise to any claim by Tenant for damages or (c) constitute a forcible or unlawful entry, a detainer or an eviction of Tenant. In the event that Landlord fails to complete the Landlord Work on or before the Term Commencement Date (as defined in Section 4.1 above), the Term Commencement Date shall be extended on a day-for-day basis until Landlord completes the Landlord Work (such that the Term Commencement Date shall be the date immediately following the day that Landlord completes the Landlord Work).

4.7 Landlord and Tenant shall mutually agree upon the selection of the architect, engineer, general contractor and major subcontractors, and Landlord and Tenant shall each participate in the review of the competitive bid process; provided that the architects, engineers, general contractors and subcontractors listed on Exhibit G attached hereto are pre-approved by Landlord for the initial Tenant Improvements. Landlord may refuse to approve any architects, consultants, contractors, subcontractors or material suppliers that Landlord reasonably believes could cause labor disharmony or may not have sufficient experience, in Landlord's reasonable opinion, to perform work in an occupied Class "A" laboratory research building and in lab areas.

4.8 Tenant shall pay all utility charges, together with any fees, surcharges and taxes thereon for the period beginning on the date that Tenant first accesses the Premises for any reason after the Execution Date.

5. Condition of Premises . Tenant acknowledges that neither Landlord nor any agent of Landlord has made any representation or warranty with respect to the condition of the Premises, the Building or the Project, or with respect to the suitability of the Premises, the Building or the Project for the conduct of Tenant's business. Tenant acknowledges that (a) it is fully familiar with the condition of the Premises and agrees to take the same in its condition "as is" as of the Execution Date and (b) Landlord shall have no obligation to alter, repair or otherwise prepare the Premises for Tenant's occupancy or to pay for or construct any improvements to the Premises, except with respect to payment of the TI Allowance. Tenant's taking of possession of the Premises shall, except as otherwise agreed to in writing by Landlord and Tenant, conclusively establish that the Premises, the Building and the Project were at such time in good, sanitary and satisfactory condition and repair.

6. Rentable Area .

6.1. The term " Rentable Area " shall reflect such areas as reasonably calculated by Landlord's architect, as the same may be reasonably adjusted from time to time by Landlord in consultation with Landlord's architect to reflect changes to the Premises, the Building or the Project, as applicable; provided that in no event will the Base Rent payable pursuant to this Lease change as a result of any remeasurement of the Premises, Building or Project, unless due to a physical change of the same.

6.2. The Rentable Area of the Building is generally determined by making separate calculations of Rentable Area applicable to each floor within the Building and totaling the Rentable Area of all floors within the Building. The Rentable Area of a floor is computed by measuring to the outside finished surface of the permanent outer Building walls. The full area

calculated as previously set forth is included as Rentable Area, without deduction for columns and projections or vertical penetrations, including stairs, elevator shafts, flues, pipe shafts, vertical ducts and the like, as well as such items' enclosing walls.

6.3. The term " Rentable Area ," when applied to the Premises, is that area equal to the usable area of the Premises, plus an equitable allocation of Rentable Area within the Building that is not then utilized or expected to be utilized as usable area, including that portion of the Building devoted to corridors, equipment rooms, restrooms, elevator lobby, atrium and mailroom.

6.4. The Rentable Area of the Project is the total Rentable Area of all buildings within the Project.

6.5. Review of allocations of Rentable Areas as between tenants of the Building and the Project shall be made as frequently as Landlord deems appropriate, including in order to facilitate an equitable apportionment of Operating Expenses (as defined below). If such review is by a licensed architect and allocations are certified by such licensed architect as being correct, then Tenant shall be bound by such certifications.

7. Rent .

7.1. Tenant shall pay to Landlord as Base Rent for the Premises, commencing on the Term Commencement Date, the sums set forth in Section 2.3 , subject to the rental adjustments provided in Article 8 hereof. Base Rent shall be paid in equal monthly installments as set forth in Section 2.3 , subject to the rental adjustments provided in Article 8 hereof, each in advance on the first day of each and every calendar month during the Term.

7.2. In addition to Base Rent, commencing on the Expense Trigger Date (as defined in Section 9.5 below), Tenant shall pay to Landlord as additional rent (" Additional Rent ") at times hereinafter specified in this Lease (a) Tenant's Adjusted Share (as defined below) of Operating Expenses (as defined below), (b) the Property Management Fee (as defined below), (c) [intentionally omitted] and (d) any other amounts that Tenant assumes or agrees to pay under the provisions of this Lease that are owed to Landlord, including any and all other sums that may become due by reason of any default of Tenant or failure on Tenant's part to comply with the agreements, terms, covenants and conditions of this Lease to be performed by Tenant, after notice and the lapse of any applicable cure periods.

7.3. Base Rent and Additional Rent shall together be denominated " Rent ." Rent shall be paid to Landlord, without abatement, deduction or offset, in lawful money of the United States of America to the address set forth in Section 2.8 or to such other person or at such other place as Landlord may from time designate in writing. In the event the Term commences or ends on a day other than the first day of a calendar month, then the Rent for such fraction of a month shall be prorated for such period on the basis of the number of days in the month and shall be paid at the then-current rate for such fractional month.

7.4. Tenant's obligation to pay Rent shall not be discharged or otherwise affected by (a) any Applicable Laws now or hereafter applicable to the Premises, (b) any other restriction on

Tenant's use, (c) except as expressly provided herein, any casualty or taking or (d) any other occurrence; and Tenant waives all rights now or hereafter existing to terminate or cancel this Lease or quit or surrender the Premises or any part thereof, or to assert any defense in the nature of constructive eviction to any action seeking to recover rent. Tenant's obligation to pay Rent with respect to any period or obligations arising, existing or pertaining to the period prior to the date of the expiration or earlier termination of the Term or this Lease shall survive any such expiration or earlier termination; provided , however, that nothing in this sentence shall in any way affect Tenant's obligations with respect to any other period.

8. Rent Adjustments . Base Rent shall be subject to an annual upward adjustment of three percent (3%) of the then-current Base Rent. The first such adjustment shall become effective commencing on the second (2 nd) annual anniversary of the Term Commencement Date, and subsequent adjustments shall become effective on every successive annual anniversary for so long as this Lease continues in effect.

9. Operating Expenses .

9.1. As used herein, the term " Operating Expenses " shall include:

(a) Government impositions, including property tax costs consisting of real and personal property taxes (including amounts due under any improvement bond upon the Building or the Project (including the parcel or parcels of real property upon which the Building, the other buildings in the Project and areas serving the Building and the Project are located)) or assessments in lieu thereof imposed by any federal, state, regional, local or municipal governmental authority, agency or subdivision (each, a " Governmental Authority "); taxes on or measured by gross rentals received from the rental of space in the Project; taxes based on the square footage of the Premises, the Building or the Project, as well as any parking charges, utilities surcharges or any other costs levied, assessed or imposed by, or at the direction of, or resulting from Applicable Laws or interpretations thereof, promulgated by any Governmental Authority in connection with the use or occupancy of the Project or the parking facilities serving the Project; taxes on this transaction or any document to which Tenant is a party creating or transferring an interest in the Premises; any fee for a business license to operate an office building; and any expenses, including the reasonable cost of attorneys or experts, reasonably incurred by Landlord in seeking reduction by the taxing authority of the applicable taxes, less tax refunds obtained as a result of an application for review thereof; and

(b) All other costs of any kind paid or incurred by Landlord in connection with the operation or maintenance of the Building and the Project (including the Amenities Building, which shall include (i) Project office rent at fair market rental for a commercially reasonable amount of space for Project management personnel located in the Amenities Building, to the extent an office used for Project operations is maintained at the Project, plus customary expenses for such office, and (ii) fair market rent for the portion of the Amenities Building used in providing the Amenities Building Services), and costs of repairs and replacements to improvements within the Project as appropriate to maintain the Project as required hereunder, including costs of funding such reasonable reserves as Landlord, consistent with good business practice, may establish to provide for future repairs and replacements, or as any Lender (as defined below) may require; costs of utilities furnished to the Common Area;

sewer fees; cable television; trash collection; cleaning, including windows (including those of the Amenities Building); heating, ventilation and air-conditioning (" HVAC "); maintenance of landscaping and grounds; snow removal; maintenance of drives and parking areas; maintenance of the roof (including that of the Amenities Building); security services and devices; building supplies; maintenance or replacement of equipment utilized for operation and maintenance of the Project; license, permit and inspection fees; sales, use and excise taxes on goods and services purchased by Landlord in connection with the operation, maintenance or repair of the Building or Project systems and equipment; telephone, postage, stationery supplies and other expenses incurred in connection with the operation, maintenance or repair of the Project; accounting, legal and other professional fees and expenses incurred in connection with the Project; costs of furniture, draperies, carpeting, landscaping supplies, snow removal and other customary and ordinary items of personal property provided by Landlord for use in Common Area or in the Project office; capital expenditures (amortized over the useful life thereof, as reasonably determined by Landlord, in accordance with generally accepted accounting principles, but in no event longer than fifteen (15) years) (any such capital expenditures, " Permitted Capital Expenditures "); costs of complying with Applicable Laws (except to the extent such costs are incurred to remedy non-compliance as of the Execution Date with Applicable Laws); costs to keep the Project in compliance with, or costs or fees otherwise required under or incurred pursuant to any CC&Rs (as defined below), including condominium fees; insurance premiums, including premiums for commercial general liability, property casualty, earthquake, terrorism and environmental coverages; portions of insured losses paid by Landlord as part of the deductible portion of a loss pursuant to the terms of insurance policies; service contracts; costs of services of independent contractors retained to do work of a nature referenced above; and costs of compensation (including employment taxes and fringe benefits) of all persons who perform regular and recurring duties connected with the day-to-day operation and maintenance of the Project, its equipment, the adjacent walks, landscaped areas, drives and parking areas, including janitors, floor waxers, window washers, watchmen, gardeners, sweepers, plow truck drivers, handymen, and engineering/maintenance/facilities personnel.

(c) Notwithstanding the foregoing, Operating Expenses shall not include any net income, franchise, capital stock, estate or inheritance taxes, or taxes that are the personal obligation of Tenant or of another tenant of the Project; any leasing commissions; expenses that relate to preparation of rental space for a tenant; expenses of initial development and construction, including grading, paving, landscaping and decorating (as distinguished from maintenance, repair and replacement of the foregoing); legal expenses relating to other tenants; costs of repairs to the extent reimbursed by payment of insurance proceeds received by Landlord; interest upon loans to Landlord or secured by a loan agreement, mortgage, deed of trust, security instrument or other loan document covering the Project or a portion thereof (collectively, "Loan Documents") (provided that interest upon a government assessment or improvement bond payable in installments shall constitute an Operating Expense under Subsection 9.1(a)); salaries of executive officers of Landlord; depreciation claimed by Landlord for tax purposes (provided that this exclusion of depreciation is not intended to delete from Operating Expenses actual costs of repairs and replacements and reasonable reserves in regard thereto that are provided for in Subsection 9.1(b)); taxes that are excluded from Operating Expenses by the last sentence of Subsection 9.1(a) ; costs or expenses incurred in connection with the financing or sale of the Project or any portion thereof; costs expressly excluded from

Operating Expenses elsewhere in this Lease or that are charged to or paid by Tenant under other provisions of this Lease; professional fees and disbursements and other costs and expenses related to the ownership (as opposed to the use, occupancy, operation, maintenance or repair) of the Project; costs incurred by Landlord due to the violation by Landlord of any law, code, regulation, ordinance or the like that would not have been incurred but for such violation; costs, including permit, license and inspection costs, incurred with respect to the installation of other tenants' or occupants' improvements made for tenants or other occupants in the Building or incurred in renovating or otherwise improving, decorating, painting or redecorating space for tenants or other occupants in the Building; expenses in connection with services or other benefits which are not offered to Tenant or for which Tenant is charged for directly but which are provided to another tenant or occupant of the Building, without charge; electric power costs or other utility costs that any tenant pays directly to the local public service company; costs (including in connection therewith all attorneys' fees) arising from claims, disputes or potential disputes in connection with potential or actual claims, litigation or arbitrations pertaining to another tenant of the Building; advertising and promotional expenses; charitable or political contributions; costs incurred in connection with the acquisition of art work (provided that costs to repair and maintain art work may be included in Operating Expenses); costs reimbursed by insurance or by other tenants of the Project; penalties, fines or interest incurred as a result of Landlord's inability or failure to make payment of taxes or other obligations of Landlord when due and/or to file any tax or informational returns when due, or from Landlord's failure to make any payment of taxes required to be made by Landlord hereunder before delinquency; bad debt loss, rent loss or reserves for bad debt or rental losses; capital expenditures other than Permitted Capital Expenditures; costs incurred to investigate, remove or remediate any Hazardous Materials (a) at the Project in violation of Applicable Laws as of the Execution Date (unless placed at the Project by a Tenant Party), (b) to the extent brought onto the Project after the Execution Date by (i) Landlord or any Landlord Parties, or (ii) a tenant at the Project other than Tenant (provided , however, in the event that Landlord is not able to determine which specific tenant brought the Hazardous Materials onto the Project, this exclusion to Operating Expenses shall not apply, provided , further, that Landlord shall use reasonable efforts to determine which specific tenant, if any, brought the Hazardous Materials onto the Project), or (c) to the extent reimbursed by payment of insurance proceeds received by Landlord; and any item that, if included in Operating Expenses, would involve a double collection for such item by Landlord. To the extent that Tenant uses more than Tenant's Pro Rata Share of any item of Operating Expenses, Tenant shall pay Landlord for such excess in addition to Tenant's obligation to pay Tenant's Pro Rata Share of Operating Expenses (such excess, together with Tenant's Pro Rata Share, " Tenant's Adjusted Share ").

9.2. Tenant shall pay to Landlord on the first day of each calendar month of the Term (and any period of occupancy prior to the Term as further described in Section 9.5), as Additional Rent, (a) the Property Management Fee (as defined below), (b) [intentionally omitted] and (c) Landlord's estimate of Tenant's Adjusted Share of Operating Expenses with respect to the Building and the Project, as applicable, for such month.

(w) The " Property Management Fee " shall equal three percent (3%) of Base Rent due from Tenant. Tenant shall pay the Property Management Fee in accordance with Section 9.2 with respect to the entire Term (and any period of occupancy prior to the Term as

further described in Section 9.5), including any extensions thereof or any holdover periods, regardless of whether Tenant is obligated to pay Base Rent, Operating Expenses or any other Rent with respect to any such period or portion thereof. For the first twelve (12) months of the Term (and any period of occupancy prior to the Term as further described in Section 9.5), the Property Management Fee shall be calculated as if Tenant were paying One Hundred Forty-Five Thousand Seven Hundred Eighty-One and 80/100 Dollars ($145,781.80) per month for Base Rent.

(x) [Intentionally omitted].

(y) Within ninety (90) days after the conclusion of each calendar year (or such longer period as may be reasonably required by Landlord), Landlord shall furnish to Tenant a statement showing in reasonable detail the actual Operating Expenses, Tenant's Adjusted Share of Operating Expenses, and the cost of providing utilities to the Premises for the previous calendar year (" Landlord's Statement "). Any additional sum due from Tenant to Landlord shall be due and payable within thirty (30) days after receipt of an invoice therefor. If the amounts paid by Tenant pursuant to this Section exceed Tenant's Adjusted Share of Operating Expenses for the previous calendar year, then Landlord shall credit the difference against the Rent next due and owing from Tenant; provided that, if the Lease term has expired, Landlord shall accompany Landlord's Statement with payment for the amount of such difference.

(z) Any amount due under this Section for any period that is less than a full month shall be prorated for such fractional month on the basis of the number of days in the month.

9.3. Landlord may, from time to time, modify Landlord's calculation and allocation procedures for Operating Expenses, so long as such modifications produce Dollar results substantially consistent with Landlord's then-current practice at the Project. Landlord or an affiliate(s) of Landlord currently own other property(ies) adjacent to the Project or its neighboring properties (collectively, " Neighboring Properties "). In connection with Landlord performing services for the Project pursuant to this Lease, similar services may be performed by the same vendor(s) for Neighboring Properties. In such a case, Landlord shall reasonably allocate to each Building and the Project the costs for such services based upon the ratio that the square footage of the Building or the Project (as applicable) bears to the total square footage of all of the Neighboring Properties or buildings within the Neighboring Properties for which the services are performed, unless the scope of the services performed for any building or property (including the Building and the Project) is disproportionately more or less than for others, in which case Landlord shall equitably allocate the costs based on the scope of the services being performed for each building or property (including the Building and the Project). Since the Project consists of multiple buildings, certain Operating Expenses may pertain to a particular building(s), certain Operating Expenses may pertain to the North Campus, and other Operating Expenses to the Project as a whole. Landlord reserves the right in its reasonable discretion to allocate in a reasonable and equitable manner any such costs applicable to any particular building within the Project to such building, any costs applicable to the North Campus to the buildings comprising the North Campus (including the Building), and other such costs applicable to the Project to each building in the Project (including the Building), with the tenants in each

building being responsible for paying their respective proportionate shares of their buildings to the extent required under their leases. Landlord shall allocate such costs to the buildings (including the Building) in a reasonable, non-discriminatory manner, and such allocation shall be binding on Tenant.

9.4. Landlord's annual statement shall be final and binding upon Tenant unless Tenant, within forty-five (45) days after Tenant's receipt thereof, shall contest any item therein by giving written notice to Landlord, specifying each item contested and the reasons therefor; provided that Tenant shall in all events pay the amount specified in Landlord's annual statement, pending the results of the Independent Review and determination of the Accountant(s), as applicable and as each such term is defined below. If, during such thirty (30)-day period, Tenant reasonably and in good faith questions or contests the correctness of Landlord's statement of Tenant's Adjusted Share of Operating Expenses, Landlord shall provide Tenant with reasonable access to Landlord's books and records to the extent relevant to determination of Operating Expenses, and such information as Landlord reasonably determines to be responsive to Tenant's written inquiries. In the event that, after Tenant's review of such information, Landlord and Tenant cannot agree upon the amount of Tenant's Adjusted Share of Operating Expenses, then Tenant shall have the right to have an independent public accounting firm hired by Tenant on an hourly basis and not on a contingent-fee basis (at Tenant's sole cost and expense) and approved by Landlord (which approval Landlord shall not unreasonably withhold or delay) audit and review such of Landlord's books and records for the year in question as directly relate to the determination of Operating Expenses for such year (the " Independent Review "), but not books and records of entities other than Landlord. Landlord shall make such books and records available at the location where Landlord maintains them in the ordinary course of its business. Landlord need not provide copies of any books or records. Tenant shall commence the Independent Review within fifteen (15) days after the date Landlord has given Tenant access to Landlord's books and records for the Independent Review. Tenant shall complete the Independent Review and notify Landlord in writing of Tenant's specific objections to Landlord's calculation of Operating Expenses (including Tenant's accounting firm's written statement of the basis, nature and amount of each proposed adjustment) no later than sixty (60) days after Landlord has first given Tenant access to Landlord's books and records for the Independent Review. Landlord shall review the results of any such Independent Review. The parties shall endeavor to agree promptly and reasonably upon Operating Expenses taking into account the results of such Independent Review. If, as of the date that is sixty (60) days after Tenant has submitted the Independent Review to Landlord, the parties have not agreed on the appropriate adjustments to Operating Expenses, then the parties shall engage a mutually agreeable independent third party accountant with at least ten (10) years' experience in commercial real estate accounting in the Newark, California area, that has not represented Landlord or Tenant in any capacity within the previous five (5) year period (the " Accountant "). If the parties cannot agree on the Accountant, each shall within ten (10) days after such impasse appoint an Accountant (different from the accountant and accounting firm that conducted the Independent Review) and, within ten (10) days after the appointment of both such Accountants, those two Accountants shall select a third (which cannot be the accountant and accounting firm that conducted the Independent Review). If either party fails to timely appoint an Accountant, then the Accountant the other party appoints shall be the sole Accountant. Within ten (10) days after appointment of the Accountant(s), Landlord and Tenant shall each simultaneously give the

Accountants (with a copy to the other party) its determination of Operating Expenses, with such supporting data or information as each submitting party determines appropriate. Within ten (10) days after such submissions, the Accountants shall by majority vote select either Landlord's or Tenant's determination of Operating Expenses. The Accountants may not select or designate any other determination of Operating Expenses. The determination of the Accountant(s) shall bind the parties. If the parties agree or the Accountant(s) determine that the Operating Expenses actually paid by Tenant for the calendar year in question exceeded Tenant's obligations for such calendar year, then Landlord shall, at Tenant's option, either (a) credit the excess to the next succeeding installments of estimated Additional Rent or (b) pay the excess to Tenant within thirty (30) days after delivery of such results. If the parties agree or the Accountant(s) determine that Tenant's payments of Operating Expenses for such calendar year were less than Tenant's obligation for the calendar year, then Tenant shall pay the deficiency to Landlord within thirty (30) days after delivery of such results. If the Independent Review reveals or the Accountant(s) determine that the Operating Expenses billed to Tenant by Landlord and paid by Tenant to Landlord for the applicable calendar year in question exceeded by more than five percent (5%) what Tenant should have been billed during such calendar year, then Landlord shall pay the reasonable cost of the Independent Review and the reasonable cost of the Accountant(s). In all other cases Tenant shall pay the cost of the Independent Review and the Accountant(s).

9.5. Tenant shall not be responsible for Operating Expenses with respect to any time period prior to the Term Commencement Date; provided , however, that if Tenant commences business operations in the Premises prior to the Term Commencement Date, Tenant shall be responsible for Operating Expenses from the date that Tenant so commences business operations in the Premises (the Term Commencement Date or such earlier date, as applicable, the " Expense Trigger Date "); and provided , further, that Landlord may annualize certain Operating Expenses incurred prior to the Expense Trigger Date over the course of the budgeted year during which the Expense Trigger Date occurs, and Tenant shall be responsible for the annualized portion of such Operating Expenses corresponding to the number of days during such year, commencing with the Expense Trigger Date, for which Tenant is otherwise liable for Operating Expenses pursuant to this Lease. Tenant's responsibility for Tenant's Adjusted Share of Operating Expenses shall continue to the later of (a) the date of termination of the Lease and (b) the date Tenant has fully vacated the Premises (provided that in the event of termination of the Lease due to a default by Tenant, Tenant's responsibility for Operating Expenses will be governed by Article 31 and not the foregoing provisions).

9.6. Operating Expenses for the calendar year in which Tenant's obligation to share therein commences and for the calendar year in which such obligation ceases shall be prorated on a basis reasonably determined by Landlord. Expenses such as taxes, assessments and insurance premiums that are incurred for an extended time period shall be prorated based upon the time periods to which they apply so that the amounts attributed to the Premises relate in a reasonable manner to the time period wherein Tenant has an obligation to share in Operating Expenses.

9.7. Within thirty (30) days after the end of each calendar month, Tenant shall submit to Landlord an invoice, or, in the event an invoice is not available, an itemized list, of all costs and expenses that (a) Tenant has incurred (either internally or by employing third parties) during the prior month and (b) for which Tenant reasonably believes it is entitled to reimbursements from Landlord pursuant to the terms of this Lease or the Work Letter.

9.8. In the event that the Building, North Campus or Project is less than fully occupied during a calendar year, Tenant acknowledges that Landlord may extrapolate Operating Expenses that vary depending on the occupancy of the Building, North Campus or Project, as applicable, to equal Landlord's reasonable estimate of what such Operating Expenses would have been, had the Building, North Campus or Project, as applicable, been ninety-five percent (95%) occupied during such calendar year; provided , however, that Landlord shall not recover more than one hundred percent (100%) of Operating Expenses.

10. Taxes on Tenant ' s Property .

10.1. Tenant shall be solely responsible for the payment of any and all taxes levied upon (a) personal property and trade fixtures located at the Premises and (b) any gross or net receipts of or sales by Tenant, and shall pay the same prior to delinquency.

10.2. If any such taxes on Tenant's personal property or trade fixtures are levied against Landlord or Landlord's property or, if the assessed valuation of the Building, the Property or the Project is increased by inclusion therein of a value attributable to Tenant's personal property or trade fixtures, and if Landlord, after written notice to Tenant, pays the taxes based upon any such increase in the assessed value of the Building, the Property or the Project, then Tenant shall, upon demand, repay to Landlord the taxes so paid by Landlord.

10.3. If any improvements in or alterations to the Premises, whether owned by Landlord or Tenant and whether or not affixed to the real property so as to become a part thereof, are assessed for real property tax purposes at a valuation higher than the valuation at which improvements conforming to Landlord's building standards (the " Building Standard ") in other spaces in the Building are assessed, then the real property taxes and assessments levied against Landlord or the Building, the Property or the Project by reason of such excess assessed valuation shall be deemed to be taxes levied against personal property of Tenant and shall be governed by the provisions of Section 10.2 . Any such excess assessed valuation due to improvements in or alterations to space in the Project leased by other tenants at the Project shall not be included in Operating Expenses. If the records of the applicable governmental assessor's office are available and sufficiently detailed to serve as a basis for determining whether such Tenant improvements or alterations are assessed at a higher valuation than the Building Standard, then such records shall be binding on both Landlord and Tenant.

11. Security Deposit .

11.1. Tenant shall deposit with Landlord on or before the Execution Date the sum set forth in Section 2.6 (the " Security Deposit "), which sum shall be held by Landlord as security for the faithful performance by Tenant of all of the terms, covenants and conditions of this Lease to be kept and performed by Tenant during the period commencing on the Execution Date and ending upon the expiration or termination of Tenant's obligations under this Lease. If Tenant Defaults (as defined below) with respect to any provision of this Lease, including any provision relating to the payment of Rent, then Landlord may (but shall not be required to) use, apply or

retain all or any part of the Security Deposit for the payment of any Rent or any other sum in default, or to compensate Landlord for any other loss or damage that Landlord may suffer by reason of Tenant's default. If any portion of the Security Deposit is so used or applied, then Tenant shall, within ten (10) days following demand therefor, deposit cash with Landlord in an amount sufficient to restore the Security Deposit to its original amount, and Tenant's failure to do so shall be a material breach of this Lease. The provisions of this Article shall survive the expiration or earlier termination of this Lease. TENANT HEREBY WAIVES THE REQUIREMENTS OF SECTION 1950.7 OF THE CALIFORNIA CIVIL CODE, AS THE SAME MAY BE AMENDED FROM TIME TO TIME.

11.2. In the event of bankruptcy or other debtor-creditor proceedings against Tenant, the Security Deposit shall be deemed to be applied first to the payment of Rent and other charges due Landlord for all periods prior to the filing of such proceedings.

11.3. Landlord may deliver to any successor-in-interest to Landlord under this Lease the funds deposited hereunder by Tenant, and thereupon Landlord shall be discharged from any further liability with respect to such deposit. This provision shall also apply to any subsequent transfers.

11.4. If Tenant shall fully and faithfully perform every provision of this Lease to be performed by it, then the Security Deposit, or any balance thereof, shall be returned to Tenant (or, at Landlord's option, to the last assignee of Tenant's interest hereunder) within thirty (30) days after the expiration or earlier termination of this Lease.

11.5. If the Security Deposit shall be in cash, Landlord shall hold the Security Deposit in an account at a banking organization selected by Landlord; provided , however, that Landlord shall not be required to maintain a separate account for the Security Deposit, but may intermingle it with other funds of Landlord. Landlord shall be entitled to all interest and/or dividends, if any, accruing on the Security Deposit. Landlord shall not be required to credit Tenant with any interest for any period during which Landlord does not receive interest on the Security Deposit.

11.6. The Security Deposit may be in the form of cash, a letter of credit or any other security instrument acceptable to Landlord in its sole discretion. Tenant may at any time, except when Tenant is in Default (as defined below), deliver a letter of credit (the " L/C Security ") as the entire Security Deposit, as follows:

(a) If Tenant elects to deliver L/C Security, then Tenant shall provide Landlord, and maintain in full force and effect throughout the Term and until the date that is ninety (90) days after the then-current Term Expiration Date, a letter of credit in the form of Exhibit E issued by an issuer reasonably satisfactory to Landlord, in the amount of the Security Deposit, with an initial term of at least one year. Landlord may require the L/C Security to be re-issued by a different issuer at any time during the Term if Landlord reasonably believes that the issuing bank of the L/C Security is or may soon become insolvent; provided, however, Landlord shall return the existing L/C Security to the existing issuer immediately upon receipt of the substitute L/C Security. If any issuer of the L/C Security shall become insolvent or placed into FDIC receivership, then Tenant shall immediately deliver to Landlord (without the

requirement of notice from Landlord) substitute L/C Security issued by an issuer reasonably satisfactory to Landlord, and otherwise conforming to the requirements set forth in this Article. As used herein with respect to the issuer of the L/C Security, "insolvent" shall mean the determination of insolvency as made by such issuer's primary bank regulator (*i.e* ., the state bank supervisor for state chartered banks; the OCC or OTS, respectively, for federally chartered banks or thrifts; or the Federal Reserve for its member banks). If, at the Term Expiration Date, any Rent remains uncalculated or unpaid, then (i) Landlord shall with reasonable diligence complete any necessary calculations, (ii) Tenant shall extend the expiry date of such L/C Security from time to time as Landlord reasonably requires and (iii) in such extended period, Landlord shall not unreasonably refuse to consent to an appropriate reduction of the L/C Security. Tenant shall reimburse Landlord's actual and reasonable legal costs in handling Landlord's acceptance of L/C Security or its replacement or extension.

(b) If Tenant delivers to Landlord satisfactory L/C Security in place of the entire Security Deposit, Landlord shall, within thirty (30) days of Tenant's written request, remit to Tenant any cash Security Deposit Landlord previously held.

(c) Landlord may draw upon the L/C Security, and hold and apply the proceeds in the same manner and for the same purposes as the Security Deposit, if (i) an uncured Default (as defined below) exists, (ii) as of the date that is forty-five (45) days before any L/C Security expires (even if such scheduled expiry date is after the Term Expiration Date) Tenant has not delivered to Landlord an amendment or replacement for such L/C Security, reasonably satisfactory to Landlord, extending the expiry date to the earlier of (1) ninety (90) days after the then-current Term Expiration Date or (2) the date that is one year after the then-current expiry date of the L/C Security, (iii) the L/C Security provides for automatic renewals, Landlord asks the issuer to confirm the current L/C Security expiry date, and the issuer fails to do so within ten (10) business days, (iv) Tenant fails to pay (when and as Landlord reasonably requires) any bank charges for Landlord's transfer of the L/C Security or (v) the issuer of the L/C Security ceases, or announces that it will cease, to maintain an office in the city where Landlord may present drafts under the L/C Security (and fails to permit drawing upon the L/C Security by overnight courier or facsimile). This Section does not limit any other provisions of this Lease allowing Landlord to draw the L/C Security under specified circumstances.

(d) Tenant shall not seek to enjoin, prevent, or otherwise interfere with Landlord's draw under L/C Security, even if it violates this Lease. Tenant acknowledges that the only effect of a wrongful draw would be to substitute a cash Security Deposit for L/C Security, causing Tenant no legally recognizable damage. Landlord shall hold the proceeds of any draw in the same manner and for the same purposes as a cash Security Deposit. In the event of a wrongful draw, the parties shall cooperate to allow Tenant to post replacement L/C Security simultaneously with the return to Tenant of the wrongfully drawn sums, and Landlord shall upon request confirm in writing to the issuer of the L/C Security that Landlord's draw was erroneous.

(e) If Landlord transfers its interest in the Premises, then Tenant shall at Tenant's expense, within five (5) business days after receiving a request from Landlord, deliver (and, if the issuer requires, Landlord shall consent to) an amendment to the L/C Security naming Landlord's grantee as substitute beneficiary. If the required Security Deposit changes while L/C Security is in force, then Tenant shall deliver (and, if the issuer requires, Landlord shall consent to) a corresponding amendment to the L/C Security.

11.7 If Tenant, as of the fourth (4th) annual anniversary of the Term Commencement Date (the "L/C Security Reduction Date"), (a) has a market capitalization of Two Hundred Fifty Million Dollars ($250,000,000) or more, and (b) has not been in Default under this Lease during the twelve (12) month period immediately preceding the L/C Security Reduction Date ((a) and (b), collectively, the "L/C Security Reduction Obligations"), then Tenant, no later than sixty (60) days after the L/C Security Reduction Date, may notify Landlord in writing that Tenant desires to reduce the Security Deposit by the L/C Security Reduction Amount (as defined below), which notification shall include (y) a certificate (in form and substance reasonably acceptable to Landlord) from Tenant's Chief Financial Officer certifying that Tenant has satisfied the L/C Security Reduction Obligations, and (z) Tenant's most recent unconsolidated financial statements audited by a nationally recognized accounting firm. If, within ten (10) business days following Landlord's receipt of such notice, Landlord reasonably determines that Tenant has met the L/C Security Reduction Obligations, then Landlord shall notify Tenant in writing and the Security Deposit shall be reduced by an amount equal to Two Hundred Twenty-Five Thousand Dollars ($225,000) (such amount, the "L/C Security Reduction Amount"), such that the amount of the required Security Deposit under the Lease shall be Two Hundred Twenty-Five Thousand Dollars ($225,000). If Landlord is holding a cash Security Deposit, then it shall return to Tenant cash in an amount equal to the L/C Security Reduction Amount within thirty (30) days of its approval of such certification. If the Security Deposit is in the form of the L/C Security, Tenant may provide to Landlord a replacement L/C Security in the amount of the reduced Security Deposit. Provided such replacement L/C Security complies with the terms and provisions of this Article 11, Landlord shall, within thirty (30) days after its receipt of such replacement L/C Security, return to Tenant the L/C Security then being held by Landlord.

12. Use.

12.1. Tenant shall use the Premises for the Permitted Use, and shall not use the Premises, or permit or suffer the Premises to be used, for any other purpose without Landlord's prior written consent, which consent Landlord may withhold in its sole and absolute discretion. During the Term, Tenant shall, subject to Force Majeure, casualty and all of the other terms, conditions and provisions of this Lease, have access to the Premises twenty-four (24) hours per day, seven (7) days per week.

12.2. Tenant shall not use or occupy the Premises in violation of Applicable Laws; zoning ordinances; or the certificate of occupancy (or its substantial equivalent) issued for the Building or the Project, and shall, upon five (5) days' written notice from Landlord, discontinue any use of the Premises that is declared or claimed by any Governmental Authority having jurisdiction to be a violation of any of the above, or that in Landlord's reasonable opinion violates any of the above. Tenant shall comply with any direction of any Governmental Authority having jurisdiction that shall, by reason of the nature of Tenant's use or occupancy of the Premises, impose any duty upon Tenant or Landlord with respect to the Premises or with respect to the use or occupation thereof, and shall indemnify, defend (at the option of and with counsel reasonably acceptable to the indemnified party(ies)), save, reimburse and hold harmless (collectively, "Indemnify," "Indemnity" or "Indemnification," as the case may require) the

Landlord and its affiliates, employees, agents and contractors; and any lender, mortgagee, ground lessor or beneficiary (each, a " Lender " and, collectively with Landlord and its affiliates, employees, agents and contractors, the " Landlord Indemnitees ") harmless from and against any and all demands, claims, liabilities, losses, costs, expenses, actions, causes of action, damages, suits or judgments, and all reasonable expenses (including reasonable attorneys' fees, charges and disbursements, regardless of whether the applicable demand, claim, action, cause of action or suit is voluntarily withdrawn or dismissed) incurred in investigating or resisting the same (collectively, " Claims ") of any kind or nature that arise before, during or after the Term as a result of Tenant's breach of this Section.

12.3. Tenant shall not do or permit to be done anything that will invalidate or increase the cost of any fire, environmental, extended coverage or any other insurance policy covering the Building or the Project, and shall comply with all rules, orders, regulations and requirements of the insurers of the Building and the Project, and Tenant shall promptly, upon demand, reimburse Landlord for any additional premium charged for such policy by reason of Tenant's failure to comply with the provisions of this Article.

12.4. Tenant shall keep all doors opening onto public corridors closed, except when in use for ingress and egress.

12.5. No additional locks or bolts of any kind shall be placed upon any of the doors or windows by Tenant, nor shall any changes be made to existing locks or the mechanisms thereof without Landlord's prior written consent, which shall not be unreasonably withheld, conditioned or delayed. Tenant shall, upon termination of this Lease, return to Landlord all keys to offices and restrooms either furnished to or otherwise procured by Tenant. In the event any key so furnished to Tenant is lost, Tenant shall pay to Landlord the cost of replacing the same or of changing the lock or locks opened by such lost key if Landlord shall deem it necessary to make such change.

12.6. No awnings or other projections shall be attached to any outside wall of the Building. No curtains, blinds, shades or screens shall be attached to or hung in, or used in connection with, any window or door of the Premises other than Landlord's standard window coverings. Neither the interior nor exterior of any windows shall be coated or otherwise sunscreened without Landlord's prior written consent, nor shall any bottles, parcels or other articles be placed on the windowsills or items attached to windows that are visible from outside the Premises. No equipment, furniture or other items of personal property shall be placed on any exterior balcony without Landlord's prior written consent.

12.7. No sign, advertisement or notice (" Signage ") shall be exhibited, painted or affixed by Tenant on any part of the Premises or the Building without Landlord's prior written consent. Signage shall conform to Landlord's design criteria. For any Signage, Tenant shall, at Tenant's own cost and expense, (a) acquire all permits for such Signage in compliance with Applicable Laws and (b) design, fabricate, install and maintain such Signage in a first-class condition. Tenant shall be responsible for reimbursing Landlord for costs incurred by Landlord in removing any of Tenant's Signage upon the expiration or earlier termination of the Lease. Interior signs on entry doors to the Premises and the directory tablet shall be inscribed, painted or affixed for Tenant by Landlord at Tenant's sole cost and expense, and shall be of a size, color

and type and be located in a place acceptable to Landlord. The directory tablet shall be provided exclusively for the display of the name and location of tenants only. Tenant shall not place anything on the exterior of the corridor walls or corridor doors other than Landlord's standard lettering. At Landlord's option, Landlord may install any Tenant Signage, and Tenant shall pay all costs associated with such installation within thirty (30) days after demand therefor.

Subject to all of the terms, conditions and provisions of this Section 12.7 , Tenant shall be entitled to install, at its sole cost and expense, a strip on the Building's monument sign (" Monument Signage "). The graphics, materials, size, color, design, lettering, lighting (if any), specifications and exact location of the Monument Signage (collectively, the " Signage Specifications ") shall be subject to the prior written approval of Landlord, which approval shall not be unreasonably withheld. In addition, the Monument Signage and all Signage Specifications therefore shall be subject to Tenant's receipt of all required governmental permits and approvals, and shall be subject to all Applicable Laws and any covenants, conditions and restrictions affecting the Project. In the event Tenant does not receive the necessary permits and approvals for the Monument Signage, Tenant's and Landlord's rights and obligations under the remaining provisions of this Lease shall not be affected. The cost of installation of the Monument Signage, as well as all costs of design and construction of such Monument Signage and all other costs associated with such Monument Signage, including, without limitation, permits, maintenance and repair, shall be the sole responsibility of Tenant. Should the Monument Signage require maintenance or repairs as determined in Landlord's reasonable judgment, Landlord shall have the right to provide written notice thereof to Tenant, and Tenant shall cause such repairs and/or maintenance to be performed within thirty (30) days after receipt of such notice from Landlord at Tenant's sole cost and expense. Should Tenant fail to perform such maintenance and repairs within the period described in the immediately preceding sentence, Landlord shall have the right to cause such work to be performed and to charge Tenant, as Additional Rent, for the cost of such work. Upon the expiration or earlier termination of this Lease, Tenant shall, at Tenant's sole cost and expense, cause the Monument Signage to be removed from the Building's monument sign and shall cause the monument sign to be restored to the condition existing prior to the placement of such Monument Signage. If Tenant fails to remove such Monument Signage and to restore the monument sign as provided in the immediately preceding sentence on or before the expiration or earlier termination of this Lease, then Landlord may perform such work, and all costs and expenses incurred by Landlord in so performing such work shall be reimbursed by Tenant to Landlord within ten (10) days after Tenant's receipt of invoice therefore. The immediately preceding sentence shall survive the expiration or earlier termination of this Lease.

The rights to the Monument Signage shall be personal to the originally named Tenant and may not be transferred. Should the name of the original Tenant change, then the Monument Signage may be modified at Tenant's sole cost and expense to reflect the new name, but only if the new name does not (i) relate to an entity that is of a character, reputation, or associated with a political orientation or a faction, that is inconsistent with the quality of the Building or would otherwise reasonably offend an institutional landlord of a project comparable to the Project, taking into consideration the level and visibility of such signage or (ii) cause Landlord to be in default under any lease or license with another tenant of the Project.

12.8. Tenant may only place equipment within the Premises with floor loading consistent with the Building's structural design unless Tenant obtains Landlord's prior written approval. Tenant may place such equipment only in a location designed to carry the weight of such equipment.

12.9. Tenant shall cause any equipment or machinery to be installed in the Premises so as to reasonably prevent sounds or vibrations therefrom from extending into the Common Area or other offices in the Project.

12.10. Tenant shall not (a) do or permit anything to be done in or about the Premises that shall in any way obstruct or interfere with the rights of other tenants or occupants of the Project, or injure or annoy them, (b) use or allow the Premises to be used for immoral, unlawful or objectionable purposes, (c) cause, maintain or permit any nuisance or waste in, on or about the Project or (d) take any other action that would in Landlord's reasonable determination in any manner adversely affect other tenants' quiet use and enjoyment of their space or adversely impact their ability to conduct business in a professional and suitable work environment. Notwithstanding anything in this Lease to the contrary, Tenant may not install any security systems (including cameras) outside the Premises or that record sounds or images outside the Premises without Landlord's prior written consent, which Landlord may withhold in its sole and absolute discretion.

12.11. Notwithstanding any other provision herein to the contrary, Tenant shall be responsible for all liabilities, costs and expenses arising out of or in connection with the compliance of the Premises with the Americans with Disabilities Act, 42 U.S.C. § 12101, et seq., and any state and local accessibility laws, codes, ordinances and rules (collectively, and together with regulations promulgated pursuant thereto, the " ADA "), and Tenant shall Indemnify the Landlord Indemnitees from and against Claims arising out of any such failure of the Premises to comply with the ADA. The Premises have not undergone inspection by a Certified Access Specialist (as defined in California Civil Code Section 55.52). A Certified Access Specialist can inspect the Premises and determine whether the Premises comply with all of the applicable construction-related accessibility standards under State law. Although State law does not require a Certified Access Specialist inspection of the Premises, Landlord may not prohibit Tenant from obtaining a Certified Access Specialist inspection of the Premises for the occupancy or potential occupancy of Tenant, if requested by Tenant. Landlord and Tenant shall agree on the arrangements for the time and manner of the Certified Access Specialist inspection, the payment of the fee for the Certified Access Specialist inspection, and the cost of making any repairs necessary to correct violations of construction-related accessibility standards within the Premises. For the avoidance of doubt, "Lenders" shall also include historic tax credit investors and new market tax credit investors. The provisions of this Section shall survive the expiration or earlier termination of this Lease.

12.12. Tenant shall maintain temperature and humidity in the Premises in accordance with ASHRAE standards at all times.

13. Rules and Regulations, CC&Rs, Parking Facilities and Common Area .

13.1. Tenant shall have the non-exclusive right, in common with others, to use the Common Area in conjunction with Tenant's use of the Premises for the Permitted Use, and such use of the Common Area and Tenant's use of the Premises shall be subject to the rules and regulations adopted by Landlord and attached hereto as Exhibit F , together with such other reasonable and nondiscriminatory rules and regulations as are hereafter promulgated by Landlord in its sole and absolute discretion (the " Rules and Regulations "); provided that any future Rules and Regulations do not materially and adversely affect Tenant's ability to use the Premises for the Permitted Use. Tenant shall and shall ensure that its contractors, subcontractors, employees, subtenants and invitees faithfully observe and comply with the Rules and Regulations. Landlord shall not be responsible to Tenant for the violation or non-performance by any other tenant or any agent, employee or invitee thereof of any of the Rules and Regulations.

13.2. This Lease is subject to any recorded covenants, conditions or restrictions on the Project or Property, as the same may be amended, amended and restated, supplemented or otherwise modified from time to time (the " CC&Rs "). Tenant shall, at its sole cost and expense, comply with the CC&Rs.

13.3. Tenant shall have a non-exclusive, irrevocable license to use Tenant's Pro Rata Share of parking facilities serving the Building in common on an unreserved basis with other tenants of the Building during the Term at no additional cost. As of the Execution Date, Tenant's Pro Rata Share of parking facilities amounts to approximately one hundred thirty-seven (137) unreserved parking spaces (i.e., 3.2 spaces per 1,000 square feet of Rentable Area within the Premises).

13.4. Tenant agrees not to unreasonably overburden the parking facilities and agrees to cooperate with Landlord and other tenants in the use of the parking facilities. Landlord reserves the right to determine that parking facilities are becoming overcrowded and to limit Tenant's use thereof; provided that in no event shall Landlord exercise such right in a manner that reduces Tenant's parking allocation below 3.2 spaces per 1,000 square feet of Rentable Area within the Premises. Upon such determination, Landlord may reasonably allocate parking spaces among Tenant and other tenants of the Building or the Project. Nothing in this Section, however, is intended to create an affirmative duty on Landlord's part to monitor parking.

14. Project Control by Landlord .

14.1. Landlord reserves full control over the Building and the Project to the extent not inconsistent with Tenant's enjoyment of the Premises as provided by this Lease. This reservation includes Landlord's right to subdivide the Project; convert the Building and other buildings within the Project to condominium units; change the size of the Project by selling all or a portion of the Project or adding real property and any improvements thereon to the Project; grant easements and licenses to third parties; maintain or establish ownership of the Building separate from fee title to the Property; make additions to or reconstruct portions of the Building and the Project; install, use, maintain, repair, replace and relocate for service to the Premises and other parts of the Building or the Project pipes, ducts, conduits, wires and appurtenant fixtures, wherever located in the Premises, the Building or elsewhere at the Project; and alter or relocate

any other Common Area or facility, including private drives, lobbies, entrances and landscaping; provided , however, that such rights shall be exercised in a way that does not materially adversely affect Tenant's beneficial use and occupancy of the Premises, including the Permitted Use and Tenant's access to the Premises. Tenant acknowledges that Landlord specifically reserves the right to allow the exclusive use of corridors and restroom facilities located on specific floors to one or more tenants occupying such floors; provided , however, that Tenant shall not be deprived of the use of the corridors reasonably required to serve the Premises or of restroom facilities serving the floor upon which the Premises are located.

14.2. Possession of areas of the Premises necessary for utilities, services, safety and operation of the Building is reserved to Landlord.

14.3. Tenant shall, at Landlord's request, promptly execute such further documents as may be reasonably appropriate to assist Landlord in the performance of its obligations hereunder; provided that Tenant need not execute any document that creates additional liability for Tenant, unreasonably diminishes Tenant's rights hereunder or that deprives Tenant of the quiet enjoyment and use of the Premises as provided for in this Lease.

14.4. Landlord may, at any and all reasonable times during non-business hours (or during business hours, if (a) with respect to Subsections 14.4(u) through 14.4(y) , Tenant so requests, and (b) with respect to Subsection 14.4(z) , if Landlord so requests), and upon twenty-four (24) hours' prior notice (which may be oral or by email to the office manager or other Tenant-designated individual at the Premises; but provided that no time restrictions shall apply or advance notice be required if an emergency necessitates immediate entry), enter the Premises to (u) inspect the same and to determine whether Tenant is in compliance with its obligations hereunder, (v) supply any service Landlord is required to provide hereunder, (w) alter, improve or repair any portion of the Building other than the Premises for which access to the Premises is reasonably necessary, (x) post notices of nonresponsibility, (y) access the telephone equipment, electrical substation and fire risers and (z) show the Premises to prospective tenants during the final year of the Term and current and prospective purchasers and lenders at any time. In connection with any such alteration, improvement or repair as described in Subsection 14.4(w) , Landlord may erect in the Premises or elsewhere in the Project scaffolding and other structures reasonably required for the alteration, improvement or repair work to be performed. In no event shall Tenant's Rent abate as a result of Landlord's activities pursuant to this Section; provided , however, that all such activities shall be conducted in such a manner so as to cause as little interference to Tenant as is reasonably possible. Landlord shall at all times retain a key with which to unlock all of the doors in the Premises. If an emergency necessitates immediate access to the Premises, Landlord may use whatever force is necessary to enter the Premises, and any such entry to the Premises shall not constitute a forcible or unlawful entry to the Premises, a detainer of the Premises, or an eviction of Tenant from the Premises or any portion thereof.

15. Quiet Enjoyment . Landlord covenants that Tenant, upon paying the Rent and performing its obligations contained in this Lease, may peacefully and quietly have, hold and enjoy the Premises, free from any claim by Landlord or persons claiming under Landlord, but subject to all of the terms and provisions hereof, provisions of Applicable Laws and rights of record to which this Lease is or may become subordinate. This covenant is in lieu of any other quiet enjoyment covenant, either express or implied.

16. Utilities and Services .

16.1. Tenant shall pay for all water (including the cost to service, repair and replace reverse osmosis, de-ionized and other treated water), gas, heat, light, power, telephone, internet service, cable television, other telecommunications and other utilities supplied to the Premises, together with any fees, surcharges and taxes thereon. If any such utility is not separately metered to Tenant, Tenant shall pay Tenant's Adjusted Share of all charges of such utility jointly metered with other premises as Additional Rent or, in the alternative, Landlord may, at its option, monitor the usage of such utilities by Tenant and charge Tenant with the cost of purchasing, installing and monitoring such metering equipment, which cost shall be paid by Tenant as Additional Rent. Landlord may base its bills for utilities on reasonable estimates; provided that Landlord adjusts such billings promptly thereafter or as part of the next Landlord's Statement to reflect the actual cost of providing utilities to the Premises. To the extent that Tenant uses more than Tenant's Pro Rata Share of any utilities, then Tenant shall pay Landlord for Tenant's Adjusted Share of such utilities to reflect such excess. In the event that the Building, North Campus or Project is less than fully occupied during a calendar year, Tenant acknowledges that Landlord may extrapolate utility usage that varies depending on the occupancy of the Building, North Campus or Project (as applicable) to equal Landlord's reasonable estimate of what such utility usage would have been had the Building, North Campus or Project, as applicable, been ninety-five percent (95%) occupied during such calendar year; provided , however, that Landlord shall not recover more than one hundred percent (100%) of the cost of such utilities.

16.2. Landlord shall not be liable for, nor shall any eviction of Tenant result from, the failure to furnish any utility or service, whether or not such failure is caused by accidents; breakage; casualties (to the extent not caused by the party claiming Force Majeure); Severe Weather Conditions (as defined below); physical natural disasters (but excluding weather conditions that are not Severe Weather Conditions); strikes, lockouts or other labor disturbances or labor disputes (other than labor disturbances and labor disputes resulting solely from the acts or omissions of the party claiming Force Majeure); acts of terrorism; riots or civil disturbances; wars or insurrections; shortages of materials (which shortages are not unique to the party claiming Force Majeure); government regulations, moratoria or other governmental actions, inactions or delays; failures to grant consent or delays in granting consent by any Lender whose consent is required under any applicable Loan Document; failures by third parties to deliver gas, oil or another suitable fuel supply, or inability of the party claiming Force Majeure, by exercise of reasonable diligence, to obtain gas, oil or another suitable fuel; or other causes beyond the reasonable control of the party claiming that Force Majeure has occurred (collectively, " Force Majeure "); or, to the extent permitted by Applicable Laws, Landlord's negligence. In the event of such failure, Tenant shall not be entitled to termination of this Lease or any abatement or reduction of Rent, nor shall Tenant be relieved from the operation of any covenant or agreement of this Lease. " Severe Weather Conditions " means weather conditions that are materially worse than those that reasonably would be anticipated for the Property at the applicable time based on historic meteorological records. In the event that the negligence or willful misconduct of Landlord (or any Landlord Party) causes an interruption of any utilities or services that Landlord must provide pursuant to this Lease, Landlord shall use commercially reasonable efforts to pursue the restoration of such utilities and/or services as soon as reasonably possible.

16.3. Tenant shall pay for, prior to delinquency of payment therefor, any utilities and services that may be furnished to the Premises during or, if Tenant occupies the Premises after the expiration or earlier termination of the Term, after the Term, beyond those utilities provided by Landlord, including telephone, internet service, cable television and other telecommunications, together with any fees, surcharges and taxes thereon. Upon Landlord's demand, utilities and services provided to the Premises that are separately metered shall be paid by Tenant directly to the supplier of such utilities or services.

16.4. Tenant shall not, without Landlord's prior written consent, use any device in the Premises (including data processing machines) that will in any way (a) increase the amount of ventilation, air exchange, gas, steam, electricity or water required or consumed in the Premises based upon Tenant's Pro Rata Share of the Building or Project (as applicable) beyond the existing capacity of the Building or the Project usually furnished or supplied for the Permitted Use or (b) exceed Tenant's Pro Rata Share of the Building's or Project's (as applicable) capacity to provide such utilities or services.

16.5. If Tenant shall require utilities or services in excess of those usually furnished or supplied for tenants in similar spaces in the Building or the Project by reason of Tenant's equipment or extended hours of business operations, then Tenant shall first procure Landlord's consent for the use thereof, which consent Landlord may condition upon the availability of such excess utilities or services, and Tenant shall pay as Additional Rent an amount equal to the cost of providing such excess utilities and services.

16.6. Landlord shall provide water in Common Area for lavatory and landscaping purposes only, which water shall be from the local municipal or similar source; provided , however, that if Landlord determines that Tenant requires, uses or consumes water provided to the Common Area for any purpose other than ordinary lavatory purposes, Landlord may install a water meter (" Tenant Water Meter ") and thereby measure Tenant's water consumption for all purposes. Tenant shall pay Landlord for the costs of any Tenant Water Meter and the installation and maintenance thereof during the Term. If Landlord installs a Tenant Water Meter, Tenant shall pay for water consumed, as shown on such meter, as and when bills are rendered. If Tenant fails to timely make such payments, Landlord may pay such charges and collect the same from Tenant. Any such costs or expenses incurred or payments made by Landlord for any of the reasons or purposes stated in this Section shall be deemed to be Additional Rent payable by Tenant and collectible by Landlord as such.

16.7. Landlord reserves the right to stop service of the elevator, plumbing, ventilation, air conditioning and utility systems (a " Service Stoppage "), when Landlord deems necessary or desirable, due to accident, emergency or the need to make repairs, alterations or improvements, until such repairs, alterations or improvements shall have been completed, and Landlord shall further have no responsibility or liability for failure to supply elevator facilities, plumbing, ventilation, air conditioning or utility service when prevented from doing so by Force Majeure or, to the extent permitted by Applicable Laws, Landlord's negligence. Without limiting the foregoing, it is expressly understood and agreed that any covenants on Landlord's part to furnish

any service pursuant to any of the terms, covenants, conditions, provisions or agreements of this Lease, or to perform any act or thing for the benefit of Tenant, shall not be deemed breached if Landlord is unable to furnish or perform the same by virtue of Force Majeure or, to the extent permitted by Applicable Laws, Landlord's negligence. Except in case of emergencies (in which event no notice shall be required), Landlord shall provide Tenant with twenty-four (24) hours' notice prior to any Service Stoppage (which notice may be oral or by email to the office manager or other Tenant-designated individual at the Premises).

16.8. As of the Execution Date, an existing back-up generator (the " Generator ") is connected to the Premises' emergency electrical panel. Landlord shall deliver the Generator to Tenant on the Execution Date in good working order, condition and repair. Except for Landlord's obligation to deliver the Generator to Tenant on the Execution Date in good working order, condition and repair (as set forth in the immediately preceding grammatical sentence), Tenant acknowledges and agrees that Landlord has made no representation or warranty (express or implied) regarding the condition of the Generator or the suitability of the Generator for Tenant's use. From and after the Execution Date, the Generator shall be the sole responsibility of Tenant and Landlord shall have no obligations with respect thereto. Tenant shall, at its sole cost and expense, maintain and keep the Generator (a) in good condition and repair, (b) in accordance with industry standard practices, (c) in compliance with all Applicable Laws (including, without limitation, any required permits); and Tenant shall otherwise be solely responsible for any repair, maintenance and/or replacement costs with respect to the Generator. If requested in writing by Landlord, Tenant shall provide to Landlord copies of any Generator maintenance contracts and any Generator maintenance reports; provided , however, that Tenant shall not be required to provide such copies to Landlord more than one (1) time per year (except that such limitation shall not apply at any time that Tenant is in Default of this Lease). Notwithstanding anything to the contrary in this Lease, Landlord shall have no liability, and Tenant shall have no right or remedy, on account of any interruption or impairment with respect to the Generator.

16.9. For the Premises, Tenant shall (subject to Landlord's obligations as set forth in Section 18.1 below) (a) maintain and operate the HVAC systems used for the Permitted Use only (" Base HVAC ") and (b) subject to Subsection 16.9(a) , furnish HVAC as reasonably required (except as this Lease otherwise provides) for reasonably comfortable occupancy of the Premises twenty-four (24) hours a day, every day during the Term, subject to casualty, eminent domain or as otherwise specified in this Article. Notwithstanding anything to the contrary in this Section, Landlord shall have no liability, and Tenant shall have no right or remedy, on account of any interruption or impairment in HVAC services. In the event of any interruption or impairment in HVAC services due to any portion of the HVAC system which Landlord is obligated to maintain hereunder, Landlord will use commercially reasonable efforts to correct such interruption or impairment as soon as reasonably possible.

16.10. For any utilities serving the Premises for which Tenant is billed directly by such utility provider, Tenant agrees to furnish to Landlord (a) any invoices or statements for such utilities within thirty (30) days after Tenant's receipt thereof, (b) within thirty (30) days after Landlord's request, any other utility usage information reasonably requested by Landlord, and (c) within thirty (30) days after each calendar year during the Term, authorization to allow Landlord to access Tenant's usage information necessary for Landlord to complete an ENERGY

STAR ® Statement of Performance (or similar comprehensive utility usage report (e.g., related to Labs 21), if requested by Landlord) and any other information reasonably requested by Landlord for the immediately preceding year; and Tenant shall comply with any other energy usage or consumption requirements required by Applicable Laws. Tenant shall retain records of utility usage at the Premises, including invoices and statements from the utility provider, throughout the Term and for such period of time after the expiration or earlier termination of this Lease as may be required in order for Landlord to comply with Applicable Laws. Tenant acknowledges that any utility information for the Premises, the Building and the Project may be shared with third parties, including Landlord's consultants and Governmental Authorities. In the event that Tenant fails to comply with this Section, Tenant hereby authorizes Landlord to collect utility usage information directly from the applicable utility providers. In addition to the foregoing, Tenant shall comply with all Applicable Laws related to the disclosure and tracking of energy consumption at the Premises. The provisions of this Section shall survive the expiration or earlier termination of this Lease.

17. Alterations .

17.1. Tenant shall make no alterations, additions or improvements other than the Tenant Improvements in or to the Premises or engage in any construction, demolition, reconstruction, renovation or other work (whether major or minor) of any kind in, at or serving the Premises (" Alterations ") without Landlord's prior written approval, which approval may be subject to the consent of one or more Lenders, if required under any applicable Loan Document, but which approval Landlord shall not otherwise unreasonably withhold; provided , however, that, in the event any proposed Alteration affects (a) any structural portions of the Building, including exterior walls, the roof, the foundation or slab, foundation or slab systems (including barriers and subslab systems) or the core of the Building, (b) the exterior of the Building or (c) any Building systems, including elevator, plumbing, HVAC, electrical, security, life safety and power, then Landlord may withhold its approval in its sole and absolute discretion. Tenant shall, in making any Alterations, use only those architects, contractors, suppliers and mechanics of which Landlord has given prior written approval, which approval shall be in Landlord's commercially reasonable discretion. In seeking Landlord's approval, Tenant shall provide Landlord, at least thirty (30) days in advance of the desired commencement date of any proposed construction, with plans, specifications, bid proposals, certified stamped engineering drawings and calculations by Tenant's engineer of record or architect of record (including connections to the Building's structural system, modifications to the Building's envelope, non-structural penetrations in slabs or walls, and modifications or tie-ins to life safety systems), work contracts, requests for laydown areas and such other information concerning the nature and cost of the Alterations as Landlord may reasonably request, provided that Tenant shall not commence any such Alterations that require Landlord's consent unless and until Tenant has received the written approval of Landlord and any and all Lenders whose consent is required under any applicable Loan Document. In no event shall Tenant use or Landlord be required to approve any architects, consultants, contractors, subcontractors or material suppliers that Landlord reasonably believes could cause labor disharmony or may not have sufficient experience, in Landlord's reasonable opinion, to perform work in an occupied Class "A" laboratory research building and in tenant-occupied lab areas.

17.2. Tenant shall not construct or permit to be constructed partitions or other obstructions that might interfere with free access to mechanical installation or service facilities of the Building or with other tenants' components located within the Building, or interfere with the moving of Landlord's equipment to or from the enclosures containing such installations or facilities.

17.3. Tenant shall accomplish any work performed on the Premises or the Building in such a manner as to permit any life safety systems to remain fully operable at all times.

17.4. Any work performed on the Premises, the Building or the Project by Tenant or Tenant's contractors shall be done at such times and in such manner as Landlord may from time to time reasonably designate; provided that Tenant will be permitted to perform Alterations during business hours so long as such Alterations do not create any noise, odors, vibration or other disturbance which (in Landlord's sole discretion) could disturb other tenants of the Building. Tenant covenants and agrees that all work done by Tenant or Tenant's contractors shall be performed in full compliance with Applicable Laws. Within thirty (30) days after completion of any Alterations, Tenant shall provide Landlord with complete "as built" drawing print sets and electronic CADD files on disc (or files in such other current format in common use as Landlord reasonably approves or requires) showing any changes in the Premises, as well as a commissioning report prepared by a licensed, qualified commissioning agent hired by Tenant and approved by Landlord for all new or affected mechanical, electrical and plumbing systems. Any such "as built" plans shall show the applicable Alterations as an overlay on the Building as-built plans; provided that Landlord provides the Building "as built" plans to Tenant.

17.5. Before commencing any Alterations or Tenant Improvements, Tenant shall (a) give Landlord at least thirty (30) days' prior written notice of the proposed commencement of such work and the names and addresses of the persons supply labor or materials therefor so that Landlord may enter the Premises to post and keep posted thereon and therein notices or to take any further action that Landlord may reasonably deem proper for the protection of Landlord's interest in the Project and (b) shall, if required by Landlord, secure, at Tenant's own cost and expense, a completion and lien indemnity bond satisfactory to Landlord for such work (provided that Landlord shall only be permitted to impose such requirement in connection with Alterations costing in excess of Seventy-Five Thousand Dollars ($75,000)).

17.6. Tenant shall repair any damage to the Premises caused by Tenant's removal of any property from the Premises. During any such restoration period, Tenant shall pay Rent to Landlord as provided herein as if such space were otherwise occupied by Tenant. The provisions of this Section shall survive the expiration or earlier termination of this Lease.

17.7. The Premises plus any Alterations; Signage; Tenant Improvements; attached equipment, decorations, fixtures and trade fixtures; laboratory casework and related appliances; and other additions and improvements attached to or built into the Premises made by either of the parties (including all floor and wall coverings; paneling; sinks and related plumbing fixtures; fixed laboratory benches; exterior venting fume hoods; walk-in freezers and refrigerators; ductwork; conduits; electrical panels and circuits; attached machinery and equipment; and built-in furniture and cabinets, in each case, together with all additions and accessories thereto), shall (unless, prior to such construction or installation, Landlord elects otherwise in writing) at all

times remain the property of Landlord, shall remain in the Premises and shall (unless, prior to construction or installation thereof, Landlord elects otherwise in writing) be surrendered to Landlord upon the expiration or earlier termination of this Lease. For the avoidance of doubt, the items listed on Exhibit H attached hereto (which Exhibit H may be updated by Tenant from and after the Term Commencement Date, subject to Landlord's written consent) constitute Tenant's property and shall be removed by Tenant upon the expiration or earlier termination of the Lease.

17.8. Notwithstanding any other provision of this Article to the contrary, in no event shall Tenant remove any improvement from the Premises in which any Lender has a security interest or as to which Landlord contributed payment, including the Tenant Improvements, without Landlord's prior written consent, which consent Landlord may withhold in its sole and absolute discretion; provided that Landlord hereby confirms that the items listed on Exhibit H remain the property of Tenant and may be removed by Tenant in its sole discretion (subject to the terms, conditions and provisions set forth in Section 17.6 above).

17.9. If Tenant shall fail to remove any of its property from the Premises prior to the expiration or earlier termination of this Lease, then Landlord may, at its option, remove the same in any manner that Landlord shall choose and store such effects without liability to Tenant for loss thereof or damage thereto, and Tenant shall pay Landlord, upon demand, any costs and expenses incurred due to such removal and storage or Landlord may, at its sole option and without notice to Tenant, sell such property or any portion thereof at private sale and without legal process for such price as Landlord may obtain and apply the proceeds of such sale against any (a) amounts due by Tenant to Landlord under this Lease and (b) any expenses incident to the removal, storage and sale of such personal property.

17.10. Tenant shall pay to Landlord an amount equal to three percent (3%) of the cost to Tenant of all Alterations to cover Landlord's overhead and expenses for plan review, engineering review, coordination, scheduling and supervision thereof or obtaining any required Lender consent. For purposes of payment of such sum, Tenant shall submit to Landlord copies of all bills, invoices and statements covering the costs of such charges, accompanied by payment to Landlord of the fee set forth in this Section. Tenant shall reimburse Landlord for any extra expenses incurred by Landlord by reason of faulty work done by Tenant or its contractors, or by reason of delays caused by such work, or by reason of inadequate clean-up.

17.11. Within sixty (60) days after final completion of any Alterations performed by Tenant with respect to the Premises, Tenant shall submit to Landlord documentation showing the amounts expended by Tenant with respect to such Alterations, together with supporting documentation reasonably acceptable to Landlord.

17.12. Tenant shall take, and shall cause its contractors to take, commercially reasonable steps to protect the Premises during the performance of any Alterations or Tenant Improvements, including covering or temporarily removing any window coverings so as to guard against dust, debris or damage.

17.13. Tenant shall require its contractors and subcontractors performing work on the Premises to name Landlord and its affiliates and Lenders as additional insureds on their respective insurance policies.

17.14. Notwithstanding anything to the contrary contained in this Lease, Tenant shall have no obligation to remove any portion of the Tenant Improvements or any subsequent Alterations approved by Landlord, unless Landlord shall have notified Tenant in writing that removal at the end of the Term would be required at the time of Landlord's consent to such Tenant Improvements or Alterations.

18. Repairs and Maintenance .

18.1. Landlord shall repair and maintain in good condition and repair the structural and exterior portions and Common Area of the Building and the Project, including roofing and covering materials; foundations (excluding any architectural slabs, but including any structural slabs); exterior walls; plumbing; fire sprinkler systems (if any); the chiller(s) located on the roof of the Building which do not exclusively serve the Premises or any other tenant's premises; elevators; and base Building electrical systems installed or furnished by Landlord.

18.2. Except for services of Landlord, if any, required by Section 18.1 , Tenant shall at Tenant's sole cost and expense maintain and keep the Premises (including but not limited to the HVAC systems serving the Premises (other than the chiller(s) to be maintained by Landlord pursuant to Section 18. 1 above), any supplemental HVAC serving the Premises, and any other systems or equipment exclusively serving the Premises) and every part thereof in good condition and repair, damage thereto from ordinary wear and tear excepted, and shall, within ten (10) days after receipt of written notice from Landlord, provide to Landlord any maintenance records that Landlord reasonably requests. Tenant shall, upon the expiration or sooner termination of the Term, surrender the Premises to Landlord in as good a condition as when received, ordinary wear and tear excepted, and with the Tenant Improvements in as good a condition as existed on the Term Commencement Date; and shall, at Landlord's request and Tenant's sole cost and expense, remove all telephone and data systems, wiring and equipment from the Premises, and repair any damage to the Premises caused thereby. Landlord shall have no obligation to alter, remodel, improve, repair, decorate or paint the Premises or any part thereof, other than pursuant to the terms and provisions of the Work Letter.

18.3. Landlord shall not be liable for any failure to make any repairs or to perform any maintenance that is Landlord's obligation pursuant to this Lease unless such failure shall persist for an unreasonable time after Tenant provides Landlord with written notice of the need of such repairs or maintenance. Tenant waives its rights under Applicable Laws now or hereafter in effect to make repairs at Landlord's expense.

18.4. If any excavation shall be made upon land adjacent to or under the Building, or shall be authorized to be made, Tenant shall afford to the person causing or authorized to cause such excavation, license to enter the Premises for the purpose of performing such work as such person shall deem necessary or desirable to preserve and protect the Building from injury or damage and to support the same by proper foundations, without any claim for damages or liability against Landlord and without reducing or otherwise affecting Tenant's obligations under this Lease. Landlord will use commercially reasonable efforts to minimize any disruption to Tenant's business operations due to work performed in accordance with this Section.

18.5. This Article relates to repairs and maintenance arising in the ordinary course of operation of the Building and the Project. In the event of a casualty described in Article 24 , Article 24 shall apply in lieu of this Article. In the event of eminent domain, Article 25 shall apply in lieu of this Article.

18.6. Costs incurred by Landlord pursuant to this Article shall constitute Operating Expenses to the extent permitted by Section 9.1.

19. Liens .

19.1. Subject to the immediately succeeding sentence, Tenant shall keep the Premises, the Building and the Project free from any liens arising out of work or services performed, materials furnished to or obligations incurred by Tenant. Tenant further covenants and agrees that any mechanic's or materialman's lien filed against the Premises, the Building or the Project for work or services claimed to have been done for, or materials claimed to have been furnished to, or obligations incurred by Tenant shall be discharged or bonded by Tenant within twenty (20) days after the filing thereof, at Tenant's sole cost and expense.

19.2. Should Tenant fail to discharge or bond against any lien of the nature described in Section 19.1 , Landlord may, at Landlord's election, pay such claim or post a statutory lien bond or otherwise provide security to eliminate the lien as a claim against title, and Tenant shall immediately reimburse Landlord for the costs thereof as Additional Rent. Tenant shall Indemnify the Landlord Indemnitees from and against any Claims arising from any such liens, including any administrative, court or other legal proceedings related to such liens.

19.3. In the event that Tenant leases or finances the acquisition of office equipment, furnishings or other personal property of a removable nature utilized by Tenant in the operation of Tenant's business, Tenant warrants that any Uniform Commercial Code financing statement shall, upon its face or by exhibit thereto, indicate that such financing statement is applicable only to removable personal property of Tenant located within the Premises. In no event shall the address of the Premises, the Building or the Project be furnished on a financing statement without qualifying language as to applicability of the lien only to removable personal property located in an identified suite leased by Tenant. Should any holder of a financing statement record or place of record a financing statement that appears to constitute a lien against any interest of Landlord or against equipment that may be located other than within an identified suite leased by Tenant, Tenant shall, within ten (10) days after filing such financing statement, cause (a) a copy of the lender security agreement or other documents to which the financing statement pertains to be furnished to Landlord to facilitate Landlord's ability to demonstrate that the lien of such financing statement is not applicable to Landlord's interest and (b) Tenant's lender to amend such financing statement and any other documents of record to clarify that any liens imposed thereby are not applicable to any interest of Landlord in the Premises, the Building or the Project.

20. Estoppel Certificate . Tenant shall, within ten (10) business days after receipt of written notice from Landlord, execute, acknowledge and deliver a statement in writing substantially in the form attached to this Lease as Exhibit I , or on any other form reasonably requested by a current or proposed Lender or encumbrancer or proposed purchaser, (a) certifying that this Lease is unmodified and in full force and effect (or, if modified, stating the nature of such modification and certifying that this Lease as so modified is in full force and effect) and the dates to which rental and other charges are paid in advance, if any, (b) acknowledging that there are not, to Tenant's knowledge, any uncured defaults on the part of Landlord hereunder, or specifying such defaults if any are claimed, and (c) setting forth such further information with respect to this Lease or the Premises as may be requested thereon. Any such statements may be relied upon by any prospective purchaser or encumbrancer of all or any portion of the Property. Tenant's failure to deliver any such statement within such the prescribed time shall, at Landlord's option, constitute a Default (as defined below) under this Lease, and, in any event, shall be binding upon Tenant that the Lease is in full force and effect and without modification except as may be represented by Landlord in any certificate prepared by Landlord and delivered to Tenant for execution.

21. Hazardous Materials .

21.1. Tenant shall not cause or permit any Hazardous Materials (as defined below) to be brought upon, kept or used in or about the Premises, the Building or the Project in violation of Applicable Laws by Tenant or any of its employees, agents, contractors or invitees (collectively with Tenant, each a " Tenant Party "). If (a) Tenant breaches such obligation, (b) the presence of Hazardous Materials as a result of such a breach results in contamination of the Project, any portion thereof, or any adjacent property, (c) contamination of the Premises otherwise occurs during the Term or any extension or renewal hereof or holding over hereunder (other than if such contamination results from migration of Hazardous Materials from outside the Premises not caused by a Tenant Party) or (d) contamination of the Project occurs as a result of Hazardous Materials that are placed on or under or are released into the Project by a Tenant Party, then Tenant shall Indemnify the Landlord Indemnitees from and against any and all Claims of any kind or nature, including (w) diminution in value of the Project or any portion thereof, (x) damages for the loss or restriction on use of rentable or usable space or of any amenity of the Project, (y) damages arising from any adverse impact on marketing of space in the Project or any portion thereof and (z) sums paid in settlement of Claims that arise before, during or after the Term as a result of such breach or contamination. This Indemnification by Tenant includes costs incurred in connection with any investigation of site conditions or any clean-up, remedial, removal or restoration work required by any Governmental Authority because of Hazardous Materials for which Tenant is responsible under the terms of this Section present in the air, soil or groundwater above, on, under or about the Project. Without limiting the foregoing, if the presence of any Hazardous Materials in, on, under or about the Project, any portion thereof or any adjacent property caused or permitted by any Tenant Party results in any contamination of the Project, any portion thereof or any adjacent property, then Tenant shall promptly take all actions at its sole cost and expense as are necessary to return the Project, any portion thereof or any adjacent property to its respective condition existing prior to the time of such contamination; provided that Landlord's written approval of such action shall first be obtained, which approval Landlord shall not unreasonably withhold; and provided , further, that it shall be reasonable for Landlord to withhold its consent if such actions could have a material adverse long-term or

short-term effect on the Project, any portion thereof or any adjacent property. Tenant's obligations under this Section shall not be affected, reduced or limited by any limitation on the amount or type of damages, compensation or benefits payable by or for Tenant under workers' compensation acts, disability benefit acts, employee benefit acts or similar legislation.

21.2. Landlord acknowledges that it is not the intent of this Article to prohibit Tenant from operating its business for the Permitted Use. Tenant may operate its business according to the custom of Tenant's industry so long as the use or presence of Hazardous Materials is strictly and properly monitored in accordance with Applicable Laws. As a material inducement to Landlord to allow Tenant to use Hazardous Materials in connection with its business, Tenant agrees to deliver to Landlord (a) a list identifying each type of Hazardous Material to be present at the Premises that is subject to regulation under any environmental Applicable Laws in the form of a Tier II form pursuant to Section 312 of the Emergency Planning and Community Right-to-Know Act of 1986 (or any successor statute) or any other form reasonably requested by Landlord, (b) a list of any and all approvals or permits from Governmental Authorities required in connection with the presence of such Hazardous Material at the Premises and (c) correct and complete copies of (i) notices of violations of Applicable Laws related to Hazardous Materials and (ii) plans relating to the installation of any storage tanks to be installed in, on, under or about the Project (provided that installation of storage tanks shall only be permitted after Landlord has given Tenant its written consent to do so, which consent Landlord may withhold in its sole and absolute discretion) and closure plans or any other documents required by any and all Governmental Authorities for any storage tanks installed in, on, under or about the Project for the closure of any such storage tanks (collectively, " Hazardous Materials Documents "). Tenant shall deliver to Landlord updated Hazardous Materials Documents, within fourteen (14) days after receipt of a written request therefor from Landlord, not more often than once per year, unless (m) there are any changes to the Hazardous Materials Documents or (n) Tenant initiates any Alterations or changes its business, in either case in a way that involves any material increase in the types or amounts of Hazardous Materials, in which case Tenant shall deliver updated Hazardous Materials documents (without Landlord having to request them) before or, if not practicable to do so before, as soon as reasonably practicable after the occurrence of the events in Subsection 21.2(m) or (n) . For each type of Hazardous Material listed, the Hazardous Materials Documents shall include (t) the chemical name, (u) the material state (e.g., solid, liquid, gas or cryogen), (v) the concentration, (w) the storage amount and storage condition (e.g., in cabinets or not in cabinets), (x) the use amount and use condition (e.g., open use or closed use), (y) the location (e.g., room number or other identification) and (z) if known, the chemical abstract service number. Notwithstanding anything in this Section to the contrary, Tenant shall not be required to provide Landlord with any documents containing information of a proprietary nature, unless such documents contain a reference to Hazardous Materials or activities related to Hazardous Materials. Landlord may, at Landlord's expense, cause the Hazardous Materials Documents to be reviewed by a person or firm qualified to analyze Hazardous Materials to confirm compliance with the provisions of this Lease and with Applicable Laws. In the event that a review of the Hazardous Materials Documents indicates non-compliance with this Lease or Applicable Laws, Tenant shall, at its expense, diligently take steps to bring its storage and use of Hazardous Materials into compliance. Notwithstanding anything in this Lease to the contrary or Landlord's review into Tenant's Hazardous Materials Documents or use or disposal of hazardous materials, however, Landlord shall not have and expressly disclaims any liability

related to Tenant's or other tenants' use or disposal of Hazardous Materials, it being acknowledged by Tenant that Tenant is best suited to evaluate the safety and efficacy of its Hazardous Materials usage and procedures.

21.3. Tenant represents and warrants to Landlord that is not nor has it been, in connection with the use, disposal or storage of Hazardous Materials, (a) subject to a material enforcement order issued by any Governmental Authority or (b) required to take any remedial action.

21.4. At any time, and from time to time, prior to the expiration of the Term, Landlord shall have the right to conduct appropriate tests of the Project or any portion thereof to demonstrate that Hazardous Materials are present or that contamination has occurred due to the acts or omissions of a Tenant Party. Tenant shall pay all reasonable costs of such tests if such tests reveal that Hazardous Materials exist at the Project as a result of a violation of this Lease by Tenant or any Tenant Party.

21.5. If underground or other storage tanks storing Hazardous Materials installed or utilized by Tenant are located on the Premises, or are hereafter placed on the Premises by Tenant (or by any other party, if such storage tanks are utilized by Tenant), then Tenant shall monitor the storage tanks, maintain appropriate records, implement reporting procedures, properly close any underground storage tanks, and take or cause to be taken all other steps necessary or required under the Applicable Laws. Tenant shall have no responsibility or liability for underground or other storage tanks installed by anyone other than Tenant unless Tenant utilizes such tanks, in which case Tenant's responsibility for such tanks shall be as set forth in this Section.

21.6. Tenant shall promptly report to Landlord any actual or suspected presence of mold or water intrusion at the Premises of which Tenant becomes aware.

21.7. Tenant's obligations under this Article shall survive the expiration or earlier termination of the Lease. During any period of time needed by Tenant or Landlord after the termination of this Lease to complete the removal from the Premises of any such Hazardous Materials, Tenant shall be deemed a holdover tenant and subject to the provisions of Article 27 .

21.8. As used herein, the term " Hazardous Material " means any toxic, explosive, corrosive, flammable, infectious, radioactive, carcinogenic, mutagenic or otherwise hazardous substance, material or waste that is or becomes regulated by Applicable Laws or any Governmental Authority.

21.9. Notwithstanding anything to the contrary in this Lease, Landlord shall have sole control over the equitable allocation of fire control areas (as defined in the Uniform Building Code as adopted by the city or municipality(ies) in which the Project is located (the " UBC ")) within the Project for the storage of Hazardous Materials. Notwithstanding anything to the contrary in this Lease, the quantity of Hazardous Materials allowed by this Section is specific to Tenant and shall not run with the Lease in the event of a Transfer (as defined in Article 29). In the event of a Transfer, if the use of Hazardous Materials by such new tenant (" New Tenant ") is such that New Tenant utilizes fire control areas in the Project in excess of New Tenant's Pro

Rata Share of the Building or the Project, as applicable, then New Tenant shall, at its sole cost and expense and upon Landlord's written request, establish and maintain a separate area of the Premises classified by the UBC as an "H" occupancy area for the use and storage of Hazardous Materials, or take such other action as is necessary to ensure that its share of the fire control areas of the Building and the Project is not greater than New Tenant's Pro Rata Share of the Building or the Project, as applicable. Notwithstanding anything in this Lease to the contrary, Landlord shall not have and expressly disclaims any liability related to Tenant's or other tenants' use or disposal of fire control areas, it being acknowledged by Tenant that Tenant and other tenants are best suited to evaluate the safety and efficacy of its Hazardous Materials usage and procedures.

22. Odors and Exhaust . Tenant acknowledges that Landlord would not enter into this Lease with Tenant unless Tenant assured Landlord that under no circumstances will any other occupants of the Building or the Project (including persons legally present in any outdoor areas of the Project) be subjected to odors or fumes (whether or not noxious), and that the Building and the Project will not be damaged by any exhaust, in each case from Tenant's operations, including in Tenant's vivarium. Landlord and Tenant therefore agree as follows:

22.1. Tenant shall not cause or permit (or conduct any activities that would cause) any release of any odors or fumes of any kind from the Premises.

22.2. If the Building has a ventilation system that, in Landlord's judgment, is adequate, suitable, and appropriate to vent the Premises in a manner that does not release odors affecting any indoor or outdoor part of the Project, Tenant shall vent the Premises through such system. If Landlord at any time reasonably determines that any existing ventilation system is inadequate, or if no ventilation system exists, Tenant shall in compliance with Applicable Laws vent all fumes and odors from the Premises (and remove odors from Tenant's exhaust stream) as Landlord reasonably requires. The placement and configuration of all ventilation exhaust pipes, louvers and other equipment shall be subject to Landlord's reasonable approval. Tenant acknowledges Landlord's legitimate desire to maintain the Project (indoor and outdoor areas) in an odor-free manner, and Landlord may require Tenant to abate and remove all odors in a manner that goes beyond the requirements of Applicable Laws.

22.3. Tenant shall, at Tenant's sole cost and expense, provide odor eliminators and other devices (such as filters, air cleaners, scrubbers and whatever other equipment may in Landlord's reasonable judgment be necessary or appropriate from time to time) to completely remove, eliminate and abate any odors, fumes or other substances in Tenant's exhaust stream that, in Landlord's judgment, emanate from Tenant's Premises. Any work Tenant performs under this Section shall constitute Alterations.

22.4. Tenant's responsibility to remove, eliminate and abate odors, fumes and exhaust shall continue throughout the Term. Landlord's approval of the Tenant Improvements shall not preclude Landlord from requiring additional measures to eliminate odors, fumes and other adverse impacts of Tenant's exhaust stream (as Landlord may reasonably designate in Landlord's reasonable discretion). Tenant shall install additional equipment as Landlord reasonably requires from time to time under the preceding sentence. Such installations shall constitute Alterations.

22.5. If Tenant fails to install satisfactory odor control equipment within ten (10) business days after Landlord's demand made at any time, then Landlord may, without limiting Landlord's other rights and remedies, require Tenant to cease and suspend any operations in the Premises that, in Landlord's reasonable determination, cause odors, fumes or exhaust. For example, if Landlord determines that Tenant's production of a certain type of product causes odors, fumes or exhaust, and Tenant does not install satisfactory odor control equipment within ten (10) business days after Landlord's request, then Landlord may require Tenant to stop producing such type of product in the Premises unless and until Tenant has installed odor control equipment satisfactory to Landlord.

23. Insurance; Waiver of Subrogation .

23.1. Landlord shall maintain insurance for the Building and the Project in amounts equal to full replacement cost (exclusive of the costs of excavation, foundations and footings, engineering costs or such other costs to the extent the same are not incurred in the event of a rebuild and without reference to depreciation taken by Landlord upon its books or tax returns) or such lesser coverage as Landlord may elect, provided that such coverage shall not be less than the amount of such insurance Landlord's Lender, if any, requires Landlord to maintain, providing protection against any peril generally included within the classification "Fire and Extended Coverage," together with insurance against sprinkler damage (if applicable), vandalism and malicious mischief. Landlord, subject to availability thereof, shall further insure, if Landlord deems it appropriate, coverage against flood, environmental hazard, earthquake, loss or failure of building equipment, rental loss during the period of repairs or rebuilding, Workers' Compensation insurance and fidelity bonds for employees employed to perform services. Notwithstanding the foregoing, Landlord may, but shall not be deemed required to, provide insurance for any improvements installed by Tenant or that are in addition to the standard improvements customarily furnished by Landlord, without regard to whether or not such are made a part of or are affixed to the Building.

23.2. In addition, Landlord shall carry Commercial General Liability insurance with limits of not less than One Million Dollars ($1,000,000) per occurrence/general aggregate for bodily injury (including death), or property damage with respect to the Project.

23.3. Tenant shall, at its own cost and expense, procure and maintain during the Term the following insurance for the benefit of Tenant and Landlord (as their interests may appear) with insurers financially acceptable and lawfully authorized to do business in the state where the Premises are located:

(a) Commercial General Liability insurance on a broad-based occurrence coverage form, with coverages including but not limited to bodily injury (including death), property damage (including loss of use resulting therefrom), premises/operations, personal & advertising injury, and contractual liability with limits of liability of not less than $2,000,000 for bodily injury and property damage per occurrence, $2,000,000 general aggregate, which limits may be met by use of excess and/or umbrella liability insurance provided that such coverage is at least as broad as the primary coverages required herein.

(b) Commercial Automobile Liability insurance covering liability arising from the use or operation of any auto, including those owned, hired or otherwise operated or used by or on behalf of the Tenant. The coverage shall be on a broad-based occurrence form with combined single limits of not less than $1,000,000 per accident for bodily injury and property damage.

(c) Commercial Property insurance covering property damage to the full replacement cost value and business interruption. Covered property shall include all tenant improvements in the Premises (to the extent not insured by Landlord pursuant to Section 23.1) and Tenant's Property including personal property, furniture, fixtures, machinery, equipment, stock, inventory and improvements and betterments, which may be owned by Tenant or Landlord and required to be insured hereunder, or which may be leased, rented, borrowed or in the care custody or control of Tenant, or Tenant's employees. Such insurance, with respect only to all Tenant Improvements, Alterations or other work performed on the Premises by Tenant (collectively, " Tenant Work "), shall name Landlord and Landlord's current and future mortgagees as loss payees as their interests may appear. Such insurance shall be written on an "all risk" of physical loss or damage basis including the perils of fire, extended coverage, electrical injury, mechanical breakdown, windstorm, vandalism, malicious mischief, sprinkler leakage, back-up of sewers or drains, flood, earthquake and such other risks Landlord may from time to time designate, for the full replacement cost value of the covered items with an agreed amount endorsement with no co-insurance. Business interruption coverage shall have limits sufficient to cover Tenant's lost profits and necessary continuing expenses, including rents due Landlord under the Lease. The minimum period of indemnity for business interruption coverage shall be twelve (12) months plus twelve (12) months' extended period of indemnity.

(d) Workers' Compensation insurance as is required by statute or law, or as may be available on a voluntary basis and Employers' Liability insurance with limits of not less than the following: each accident, Five Hundred Thousand Dollars ($500,000); disease ($500,000); disease (each employee), Five Hundred Thousand Dollars ($500,000).

(e) Medical malpractice insurance at limits of not less than $1,000,000 each claim during such periods, if any, that Tenant engages in the practice of medicine at the Premises. For avoidance of doubt, Tenant shall not be required to carry the foregoing medical malpractice insurance so long as Tenant is not (i) treating patients at the Premises, (ii) conducting clinical trials on human beings at the Premises or (iii) otherwise engaging in the practice of medicine at the Premises.

(f) Pollution Legal Liability insurance is required if Tenant stores, handles, generates or treats Hazardous Materials, as determined solely by Landlord, on or about the Premises. Such coverage shall include bodily injury, sickness, disease, death or mental anguish or shock sustained by any person; property damage including physical injury to or destruction of tangible property including the resulting loss of use thereof, clean-up costs, and the loss of use of tangible property that has not been physically injured or destroyed; and defense costs, charges and expenses incurred in the investigation, adjustment or defense of claims for such compensatory damages. Coverage shall apply to both sudden and non-sudden pollution conditions including the discharge, dispersal, release or escape of smoke, vapors, soot, fumes, acids, alkalis, toxic chemicals, liquids or gases, waste materials or other irritants, contaminants

or pollutants into or upon land, the atmosphere or any watercourse or body of water. Claims-made coverage is permitted, provided the policy retroactive date is continuously maintained prior to the commencement date of this agreement, and coverage is continuously maintained during all periods in which Tenant occupies the Premises. Coverage shall be maintained with limits of not less than $1,000,000 per incident with a $2,000,000 policy aggregate and for a period of two (2) years thereafter.

(g) During all construction by Tenant at the Premises, with respect to tenant improvements being constructed (including the Tenant Improvements and any Alterations, insurance required in Exhibit B-1 must be in place.

23.4. The insurance required of Tenant by this Article shall be with companies at all times having a current rating of not less than A- and financial category rating of at least Class VII in "A.M. Best's Insurance Guide" current edition. Tenant shall obtain for Landlord from the insurance companies/broker or cause the insurance companies/broker to furnish certificates of insurance evidencing all coverages required herein to Landlord. Tenant shall give twenty (20) days' prior written notice to Landlord if any such policy is to be cancelled or reduced below the coverage requirements of this Article (except in the event of non-payment of premium, in which case ten (10) days' written notice shall be given). All such policies shall be written as primary policies, not contributing with and not in excess of the coverage that Landlord may carry. Tenant's required policies shall contain severability of interests clauses stating that, except with respect to limits of insurance, coverage shall apply separately to each insured or additional insured. Tenant shall, at least twenty-five (25) days prior to the expiration of such policies, furnish Landlord with renewal certificates of insurance or binders. Tenant agrees that if Tenant does not take out and maintain such insurance, Landlord may (but shall not be required to) procure such insurance on Tenant's behalf and at its cost to be paid by Tenant as Additional Rent. Commercial General Liability, Commercial Automobile Liability, Umbrella Liability and Pollution Legal Liability insurance as required above shall name Landlord, BioMed Realty, L.P., and BRE Edison Parent L.P., and their respective officers, employees, agents, general partners, members, subsidiaries, affiliates and Lenders (" Landlord Parties ") as additional insureds as respects liability arising from work or operations performed by or on behalf of Tenant, Tenant's use or occupancy of Premises, and ownership, maintenance or use of vehicles by or on behalf of Tenant.

23.5. In each instance where insurance is to name Landlord Parties as additional insureds, Tenant shall, upon Landlord's written request, also designate and furnish certificates evidencing such Landlord Parties as additional insureds to (a) any Lender of Landlord holding a security interest in the Building or the Project, (b) the landlord under any lease whereunder Landlord is a tenant of the real property upon which the Building is located if the interest of Landlord is or shall become that of a tenant under a ground lease rather than that of a fee owner and (c) any management company retained by Landlord to manage the Project.

23.6. Tenant assumes the risk of damage to any fixtures, goods, inventory, merchandise, equipment and leasehold improvements, and Landlord shall not be liable for injury to Tenant's business or any loss of income therefrom, relative to such damage, all as more particularly set forth within this Lease. Tenant shall, at Tenant's sole cost and expense, carry such insurance as Tenant desires for Tenant's protection with respect to personal property of Tenant or business interruption.

23.7. Tenant and its insurers hereby waive any and all rights of recovery or subrogation against the Landlord Parties with respect to any loss, damage, claims, suits or demands, howsoever caused, that are covered, or should have been covered, by valid and collectible insurance, including any deductibles or self-insurance maintained thereunder. If necessary, Tenant agrees to endorse the required insurance policies to permit waivers of subrogation as required hereunder and hold harmless and indemnify the Landlord Parties for any loss or expense incurred as a result of a failure to obtain such waivers of subrogation from insurers. Such waivers shall continue so long as Tenant's insurers so permit. Any termination of such a waiver shall be by written notice to Landlord, containing a description of the circumstances hereinafter set forth in this Section. Tenant, upon obtaining the policies of insurance required or permitted under this Lease, shall give notice to its insurance carriers that the foregoing waiver of subrogation is contained in this Lease. If such policies shall not be obtainable with such waiver or shall be so obtainable only at a premium over that chargeable without such waiver, then Tenant shall notify Landlord of such conditions.

23.8. Landlord may require insurance policy limits required under this Lease to be raised to conform with requirements of Landlord's Lender.

23.9. Any costs incurred by Landlord pursuant to this Article shall constitute a portion of Operating Expenses.

23.10. The provisions of this Article shall survive the expiration or earlier termination of this Lease.

24. Damage or Destruction .

24.1. In the event of a partial destruction of (a) the Premises, (b) the Building, (c) the Common Area or (d) the Project ((a)-(d) collectively, the " Affected Areas ") by fire or other perils covered by extended coverage insurance not exceeding twenty-five percent (25%) of the full insurable value thereof, and provided that (w) the damage thereto is such that the Affected Areas may be repaired, reconstructed or restored within a period of six (6) months from the date of the happening of such casualty, (x) Landlord shall receive insurance proceeds from its insurer or Lender sufficient to cover the cost of such repairs, reconstruction and restoration (except for any deductible amount provided by Landlord's policy, which deductible amount, if paid by Landlord, shall constitute an Operating Expense), (y) the repair, reconstruction or restoration of the Affected Areas is permitted by all applicable Loan Documents or otherwise consented to by any and all Lenders whose consent is required thereunder, and (z) such casualty was not intentionally caused by a Tenant Party, then Landlord shall commence and proceed diligently with the work of repair, reconstruction and restoration of the Affected Areas and this Lease shall continue in full force and effect.

24.2. In the event of any damage to or destruction of the Building or the Project other than as described in Section 24.1 , Landlord may elect to repair, reconstruct and restore the Building or the Project, as applicable, in which case this Lease shall continue in full force and

effect. If Landlord elects not to repair, reconstruct and restore the Building or the Project, as applicable, then this Lease shall terminate as of the date of such damage or destruction. In the event of any damage or destruction (regardless of whether such damage is governed by Section 24.1 or this Section), if (a) in Landlord's determination as set forth in the Damage Repair Estimate (as defined below), the Affected Areas cannot be repaired, reconstructed or restored within twelve (12) months after the date of the Damage Repair Estimate, (b) subject to Section 24.6 , the Affected Areas are not actually repaired, reconstructed and restored within eighteen (18) months after the date of the Damage Repair Estimate, or (c) the damage and destruction occurs within the last twelve (12) months of the then-current Term, then Tenant shall have the right to terminate this Lease, effective as of the date of such damage or destruction, by delivering to Landlord its written notice of termination (a " Termination Notice ") (y) with respect to Subsections 24.2(a) and (c) , no later than fifteen (15) days after Landlord delivers to Tenant Landlord's Damage Repair Estimate and (z) with respect to Subsection 24.2(b) , no later than fifteen (15) days after such eighteen (18) month period (as the same may be extended pursuant to Section 24.6) expires. If Tenant provides Landlord with a Termination Notice pursuant to Subsection 24.2(z) , Landlord shall have an additional thirty (30) days after receipt of such Termination Notice to complete the repair, reconstruction and restoration. If Landlord does not complete such repair, reconstruction and restoration within such thirty (30) day period, then Tenant may terminate this Lease by giving Landlord written notice within two (2) business days after the expiration of such thirty (30) day period. If Landlord does complete such repair, reconstruction and restoration within such thirty (30) day period, then this Lease shall continue in full force and effect.

24.3. As soon as reasonably practicable, but in any event within sixty (60) days following the date of damage or destruction, Landlord shall notify Tenant of Landlord's good faith estimate of the period of time in which the repairs, reconstruction and restoration will be completed (the " Damage Repair Estimate "), which estimate shall be based upon the opinion of a contractor reasonably selected by Landlord and experienced in comparable repair, reconstruction and restoration of similar buildings. Additionally, Landlord shall give written notice to Tenant within sixty (60) days following the date of damage or destruction of its election not to repair, reconstruct or restore the Building or the Project, as applicable.

24.4. Upon any termination of this Lease under any of the provisions of this Article, the parties shall be released thereby without further obligation to the other from the date possession of the Premises is surrendered to Landlord, except with regard to (a) items occurring prior to the damage or destruction and (b) provisions of this Lease that, by their express terms, survive the expiration or earlier termination hereof.

24.5. In the event of repair, reconstruction and restoration as provided in this Article, all Rent to be paid by Tenant under this Lease shall be abated proportionately based on the extent to which Tenant's use of the Premises is impaired during the period of such repair, reconstruction or restoration, unless Landlord provides Tenant with other space during the period of repair, reconstruction and restoration that, in Tenant's reasonable opinion, is suitable for the temporary conduct of Tenant's business; provided , however, that the amount of such abatement shall be reduced by the amount of Rent that is received by Tenant as part of the business interruption or loss of rental income with respect to the Premises from the proceeds of business interruption or loss of rental income insurance.

24.6. Notwithstanding anything to the contrary contained in this Article, (a) Landlord shall not be required to repair, reconstruct or restore any damage or destruction to the extent that Landlord is prohibited from doing so by any applicable Loan Document or any Lender whose consent is required thereunder withholds its consent, and (b) should Landlord be delayed or prevented from completing the repair, reconstruction or restoration of the damage or destruction to the Premises after the occurrence of such damage or destruction by Force Majeure or delays caused by a Lender or Tenant Party, then the time for Landlord to commence or complete repairs, reconstruction and restoration shall be extended on a day-for-day basis; provided , however, that, at Landlord's election in the event of an occurrence under clause (b), Landlord shall be relieved of its obligation to make such repairs, reconstruction and restoration upon Landlord's delivery of written notice to Tenant.

24.7. If Landlord is obligated to or elects to repair, reconstruct or restore as herein provided, then Landlord shall be obligated to make such repairs, reconstruction or restoration only with regard to (a) those portions of the Premises that were originally provided at Landlord's expense and (b) the Common Area portion of the Affected Areas. The repairs, reconstruction or restoration of improvements not originally provided by Landlord or at Landlord's expense shall be the obligation of Tenant. In the event Tenant has elected to upgrade certain improvements from the Building Standard, Landlord shall, upon the need for replacement due to an insured loss, provide only the Building Standard, unless Tenant again elects to upgrade such improvements and pay any incremental costs related thereto, except to the extent that excess insurance proceeds, if received, are adequate to provide such upgrades, in addition to providing for basic repairs, reconstruction and restoration of the Premises, the Building and the Project.

24.8. Notwithstanding anything to the contrary contained in this Article, Landlord shall not have any obligation whatsoever to repair, reconstruct or restore the Premises if the damage resulting from any casualty covered under this Article occurs during the last twelve (12) months of the Term or any extension thereof, or to the extent that insurance proceeds are not available therefor.

24.9. Landlord's obligation, should it elect or be obligated to repair, reconstruct or restore, shall be limited to the Affected Areas, and shall be conditioned upon Landlord receiving any permits or authorizations required by Applicable Laws. Tenant shall, at its expense, replace or fully repair all of Tenant's personal property and any Alterations installed by Tenant existing at the time of such damage or destruction. If Affected Areas are to be repaired, reconstructed or restored in accordance with the foregoing, Landlord shall make available to Tenant any portion of insurance proceeds it receives that are allocable to the Alterations constructed by Tenant pursuant to this Lease; provided Tenant is not then in default under this Lease, and subject to the requirements of any Lender of Landlord.

24.10. This Article sets forth the terms and conditions upon which this Lease may terminate in the event of any damage or destruction. Accordingly, the parties hereby waive the provisions of California Civil Code Sections 1932(2) and 1933(4) (and any successor statutes) permitting the parties to terminate this Lease as a result of any damage or destruction.

25. Eminent Domain .

25.1. In the event (a) the whole of all Affected Areas or (b) such part thereof as shall substantially interfere with Tenant's use and occupancy of the Premises for the Permitted Use shall be taken for any public or quasi-public purpose by any lawful power or authority by exercise of the right of appropriation, condemnation or eminent domain, or sold to prevent such taking, Tenant or Landlord may terminate this Lease effective as of the date possession is required to be surrendered to such authority, except with regard to (y) items occurring prior to the taking and (z) provisions of this Lease that, by their express terms, survive the expiration or earlier termination hereof.

25.2. In the event of a partial taking of (a) the Building or the Project or (b) drives, walkways or parking areas serving the Building or the Project for any public or quasi-public purpose by any lawful power or authority by exercise of right of appropriation, condemnation, or eminent domain, or sold to prevent such taking, then, without regard to whether any portion of the Premises occupied by Tenant was so taken, Landlord may elect to terminate this Lease (except with regard to (y) items occurring prior to the taking and (z) provisions of this Lease that, by their express terms, survive the expiration or earlier termination hereof) as of such taking if such taking is, in Landlord's sole opinion, of a material nature such as to make it uneconomical to continue use of the unappropriated portion for the Permitted Use.

25.3. To the extent permitted under all applicable Loan Documents or otherwise consented to by any and all Lenders whose consent is required thereunder, Tenant shall be entitled to any award that is specifically awarded as compensation for (a) the taking of Tenant's personal property that was installed at Tenant's expense and (b) the costs of Tenant moving to a new location. Except as set forth in the previous sentence, any award for such taking shall be the property of Landlord.

25.4. If, upon any taking of the nature described in this Article, this Lease continues in effect, then Landlord shall promptly proceed to restore the Affected Areas to substantially their same condition prior to such partial taking. To the extent such restoration is infeasible, as determined by Landlord in its sole and absolute discretion, the Rent shall be decreased proportionately to reflect the loss of any portion of the Premises no longer available to Tenant. Notwithstanding anything to the contrary contained in this Article, Landlord shall not be required to restore the Affected Areas to the extent that Landlord is prohibited from doing so by any applicable Loan Document or any Lender whose consent is required thereunder withholds its consent.

25.5. This Article sets forth the terms and conditions upon which this Lease may terminate in the event of any damage or destruction. Accordingly, the parties hereby waive the provisions of California Code of Civil Procedure Section 1265.130 (and any successor statutes) permitting the parties to terminate this Lease as a result of any damage or destruction.

26. Surrender .

26.1. At least thirty (30) days prior to Tenant's surrender of possession of any part of the Premises, Tenant shall provide Landlord with a facility decommissioning and Hazardous Materials closure plan for the Premises (" Exit Survey ") prepared by an independent third party

state-certified professional with appropriate expertise, which Exit Survey must be reasonably acceptable to Landlord. The Exit Survey shall comply with the American National Standards Institute's Laboratory Decommissioning guidelines (ANSI/AIHA Z9.11-2008) or any successor standards published by ANSI or any successor organization (or, if ANSI and its successors no longer exist, a similar entity publishing similar standards). In addition, prior to, and as a condition to, Tenant's surrender of possession of any part of the Premises, Tenant shall (a) provide Landlord with written evidence of all appropriate governmental releases obtained by Tenant in accordance with Applicable Laws, including laws pertaining to the surrender of the Premises, (b) place Laboratory Equipment Decontamination Forms on all decommissioned equipment to assure safe occupancy by future users and (c) conduct a site inspection with Landlord. In addition, Tenant agrees to remain responsible after the surrender of the Premises for the remediation of any recognized environmental conditions set forth in the Exit Survey (for which Tenant is responsible pursuant to the terms of this Lease) and comply with any recommendations set forth in the Exit Survey. During any period of time needed after the expiration or earlier termination of this Lease to complete the requirements set forth in this Section, Tenant shall be deemed a holdover tenant and subject to the provisions of Article 27 . Tenant's obligations under this Section shall survive the expiration or earlier termination of the Lease.

26.2. No surrender of possession of any part of the Premises shall release Tenant from any of its obligations hereunder, unless such surrender is accepted in writing by Landlord.

26.3. The voluntary or other surrender of this Lease by Tenant shall not effect a merger with Landlord's fee title or leasehold interest in the Premises, the Building, the Property or the Project, unless Landlord consents in writing, and shall, at Landlord's option, operate as an assignment to Landlord of any or all subleases.

26.4. The voluntary or other surrender of any ground or other underlying lease that now exists or may hereafter be executed affecting the Building or the Project, or a mutual cancellation thereof or of Landlord's interest therein by Landlord and its lessor shall not effect a merger with Landlord's fee title or leasehold interest in the Premises, the Building or the Property and shall, at the option of the successor to Landlord's interest in the Building or the Project, as applicable, operate as an assignment of this Lease.

27. Holding Over .

27.1. If, with Landlord's prior written consent, Tenant holds possession of all or any part of the Premises after the Term, Tenant shall become a tenant from month to month after the expiration or earlier termination of the Term, and in such case Tenant shall continue to pay (a) Base Rent in accordance with Article 7 , as adjusted in accordance with Article 8 , and (b) any amounts for which Tenant would otherwise be liable under this Lease if the Lease were still in effect, including payments for Tenant's Adjusted Share of Operating Expenses. Any such month-to-month tenancy shall be subject to every other term, covenant and agreement contained herein.

27.2. Notwithstanding the foregoing, if Tenant remains in possession of the Premises after the expiration or earlier termination of the Term without Landlord's prior written consent,

(a) Tenant shall become a tenant at sufferance subject to the terms and conditions of this Lease, except that the monthly rent shall be equal to one hundred fifty percent (150%) of the Rent in effect during the last thirty (30) days of the Term, and (b) Tenant shall be liable to Landlord for any and all damages suffered by Landlord as a result of such holdover, including any lost rent or consequential, special and indirect damages (in each case, regardless of whether such damages are foreseeable).

27.3. Acceptance by Landlord of Rent after the expiration or earlier termination of the Term shall not result in an extension, renewal or reinstatement of this Lease.

27.4. The foregoing provisions of this Article are in addition to and do not affect Landlord's right of reentry or any other rights of Landlord hereunder or as otherwise provided by Applicable Laws.

27.5. The provisions of this Article shall survive the expiration or earlier termination of this Lease.

28. Indemnification and Exculpation .

28.1. Tenant agrees to Indemnify the Landlord Indemnitees from and against any and all Claims of any kind or nature, real or alleged, arising from (a) injury to or death of any person or damage to any property occurring within or about the Premises, the Building, the Property or the Project, arising directly or indirectly out of (i) the presence at or use or occupancy of the Premises or Project by a Tenant Party, (ii) an act or omission on the part of any Tenant Party, (b) a breach or default by Tenant in the performance of any of its obligations hereunder (including any Claim asserted by any Lender against any Landlord Indemnitees under any Loan Document as a direct result of such breach or default by Tenant) or (c) injury to or death of persons or damage to or loss of any property, real or alleged, arising from the serving of alcoholic beverages at the Premises or Project, including liability under any dram shop law, host liquor law or similar Applicable Law, except to the extent directly caused by Landlord's negligence or willful misconduct. Tenant's obligations under this Section shall not be affected, reduced or limited by any limitation on the amount or type of damages, compensation or benefits payable by or for Tenant under workers' compensation acts, disability benefit acts, employee benefit acts or similar legislation. Tenant's obligations under this Section shall survive the expiration or earlier termination of this Lease.

28.2. Notwithstanding anything in this Lease to the contrary, Landlord shall not be liable to Tenant for and Tenant assumes all risk of (a) damage or losses caused by fire, electrical malfunction, gas explosion or water damage of any type (including broken water lines, malfunctioning fire sprinkler systems, roof leaks or stoppages of lines), unless any such loss is due to Landlord's willful disregard of written notice by Tenant of need for a repair that Landlord is responsible to make for an unreasonable period of time, and (b) damage to personal property or scientific research, including loss of records kept by Tenant within the Premises (in each case, regardless of whether such damages are foreseeable). Tenant further waives any claim for injury to Tenant's business or loss of income relating to any such damage or destruction of personal property as described in this Section. Notwithstanding anything in the foregoing or this Lease to the contrary, except (x) as otherwise provided herein (including Section 27.2), (y) as may be

provided by Applicable Laws or (z) in the event of Tenant's breach of Article 21 or Section 26.1 , in no event shall Landlord or Tenant be liable to the other for any consequential, special or indirect damages arising out of this Lease, including lost profits (provided that this Subsection 28.2(z) shall not limit Tenant's liability for Base Rent or Additional Rent pursuant to this Lease).

28.3. Landlord and the Landlord Parties shall not be liable for any damages arising from any act, omission or neglect of any other tenant in the Building or the Project, or of any other third party.

28.4. Tenant acknowledges that security devices and services, if any, while intended to deter crime, may not in given instances prevent theft or other criminal acts. Landlord shall not be liable for injuries or losses caused by criminal acts of third parties, and Tenant assumes the risk that any security device or service may malfunction or otherwise be circumvented by a criminal. If Tenant desires protection against such criminal acts, then Tenant shall, at Tenant's sole cost and expense, obtain appropriate insurance coverage. Tenant's security programs and equipment for the Premises shall be coordinated with Landlord and subject to Landlord's reasonable approval.

28.5. The provisions of this Article shall survive the expiration or earlier termination of this Lease.

29. Assignment or Subletting .

29.1. Except as hereinafter expressly permitted, none of the following (each, a " Transfer "), either voluntarily or by operation of Applicable Laws, shall be directly or indirectly performed without Landlord's prior written consent: (a) Tenant selling, hypothecating, assigning, pledging, encumbering or otherwise transferring this Lease or subletting the Premises or (b) a controlling interest in Tenant being sold, assigned or otherwise transferred (other than as a result of shares in Tenant being sold on a public stock exchange). For purposes of the preceding sentence, "control" means (a) owning (directly or indirectly) more than fifty percent (50%) of the stock or other equity interests of another person or (b) possessing, directly or indirectly, the power to direct or cause the direction of the management and policies of such person. Notwithstanding the foregoing, Tenant shall have the right to Transfer, without Landlord's prior written consent, Tenant's interest in this Lease or the Premises or any part thereof to any person that (i) acquires all or substantially all of the assets of Tenant, (ii) is a successor to Tenant by merger, consolidation or reorganization, or (iii) as of the date of determination and at all times thereafter directly, or indirectly through one or more intermediaries, controls, is controlled by or is under common control with Tenant (any person described in (i), (ii), or (iii), a " Tenant's Affiliate "); provided that Tenant shall notify Landlord in writing at least ten (10) business days prior to the effectiveness of such Transfer to Tenant's Affiliate (an " Exempt Transfer ") and otherwise comply with the requirements of this Lease regarding such Transfer; and provided , further, that the person that will be the tenant under this Lease after the Exempt Transfer has a net worth (as of both the day immediately prior to and the day immediately after the Exempt Transfer) that is equal to or greater than the greater of (x) the net worth of the transferring Tenant as of the Execution Date, and (z) the lesser of (i) the net worth of the Transferring Tenant as of the date of the Exempt Transfer, and (ii) a net worth of Five Hundred Million Dollars ($500,000,000). For purposes of the immediately preceding

sentence, "control" requires both (a) owning (directly or indirectly) more than fifty percent (50%) of the stock or other equity interests of another person and (b) possessing, directly or indirectly, the power to direct or cause the direction of the management and policies of such person. In no event shall Tenant perform a Transfer to or with an entity that is a tenant at the Project or that is in discussions or negotiations with Landlord or an affiliate of Landlord to lease premises at the Project or a property owned by Landlord or an affiliate of Landlord. Notwithstanding anything in this Lease to the contrary, if (a) Tenant or any proposed transferee, assignee or sublessee of Tenant has been required by any prior landlord, Lender or Governmental Authority to take material remedial action in connection with Hazardous Materials contaminating a property if the contamination resulted from such party's action or omission or use of the property in question or (b) Tenant or any proposed transferee, assignee or sublessee is subject to a material enforcement order issued by any Governmental Authority in connection with the use, disposal or storage of Hazardous Materials, then Landlord shall have the right to terminate this Lease in Landlord's sole and absolute discretion (with respect to any such matter involving Tenant), and it shall not be unreasonable for Landlord to withhold its consent to any proposed transfer, assignment or subletting (with respect to any such matter involving a proposed transferee, assignee or sublessee).

29.2. In the event Tenant desires to effect a Transfer, then, at least thirty (30) but not more than ninety (90) days prior to the date when Tenant desires the Transfer to be effective (the " Transfer Date "), Tenant shall provide written notice to Landlord (the " Transfer Notice ") containing information (including references) concerning the character of the proposed transferee, assignee or sublessee; the Transfer Date; the most recent unconsolidated financial statements of Tenant and of the proposed transferee, assignee or sublessee satisfying the requirements of Section 40.2 (" Required Financials "); any ownership or commercial relationship between Tenant and the proposed transferee, assignee or sublessee; copies of Hazardous Materials Documents for the proposed transferee, assignee or sublessee; and the consideration and all other material terms and conditions of the proposed Transfer, all in such detail as Landlord shall reasonably require.

29.3. Landlord, in determining whether consent should be given to a proposed Transfer, may give consideration to (a) the financial strength of Tenant and of such transferee, assignee or sublessee (notwithstanding Tenant remaining liable for Tenant's performance), (b) any change in use that such transferee, assignee or sublessee proposes to make in the use of the Premises and (c) Landlord's desire to exercise its rights under Section 29.7 to cancel this Lease. In no event shall Landlord be deemed to be unreasonable for declining to consent to a Transfer if any applicable Loan Document prohibits such assignment or any Lender whose consent is required thereunder withholds its consent, or if the Transfer is to a transferee, assignee or sublessee of poor reputation, lacking financial qualifications or seeking a change in the Permitted Use, or jeopardizing directly or indirectly the status of Landlord or any of Landlord's affiliates as a Real Estate Investment Trust under the Internal Revenue Code of 1986 (as the same may be amended from time to time, the " Revenue Code "). Notwithstanding anything contained in this Lease to the contrary, (w) no Transfer shall be consummated on any basis such that the rental or other amounts to be paid by the occupant, assignee, manager or other transferee thereunder would be based, in whole or in part, on the income or profits derived by the business activities of such occupant, assignee, manager or other transferee; (x) Tenant shall not furnish or render any

services to an occupant, assignee, manager or other transferee with respect to whom transfer consideration is required to be paid, or manage or operate the Premises or any capital additions so transferred, with respect to which transfer consideration is being paid; (y) Tenant shall not consummate a Transfer with any person in which Landlord owns an interest, directly or indirectly (by applying constructive ownership rules set forth in Section 856(d)(5) of the Revenue Code); and (z) Tenant shall not consummate a Transfer with any person or in any manner that could cause any portion of the amounts received by Landlord pursuant to this Lease or any sublease, license or other arrangement for the right to use, occupy or possess any portion of the Premises to fail to qualify as "rents from real property" within the meaning of Section 856(d) of the Revenue Code, or any similar or successor provision thereto or which could cause any other income of Landlord to fail to qualify as income described in Section 856(c)(2) of the Revenue Code.

29.4. The following are conditions precedent to a Transfer or to Landlord considering a request by Tenant to a Transfer:

(a) Tenant shall remain fully liable under this Lease. Tenant agrees that it shall not be (and shall not be deemed to be) a guarantor or surety of this Lease, however, and waives its right to claim that is it is a guarantor or surety or to raise in any legal proceeding any guarantor or surety defenses permitted by this Lease or by Applicable Laws;

(b) If Tenant or the proposed transferee, assignee or sublessee does not or cannot deliver the Required Financials, then Landlord may elect to have either Tenant's ultimate parent company or the proposed transferee's, assignee's or sublessee's ultimate parent company provide a guaranty of the applicable entity's obligations under this Lease, in a form acceptable to Landlord, which guaranty shall be executed and delivered to Landlord by the applicable guarantor prior to the Transfer Date;

(c) In the case of an Exempt Transfer, Tenant shall provide Landlord with evidence reasonably satisfactory to Landlord that the Transfer qualifies as an Exempt Transfer;

(d) Tenant shall provide Landlord with evidence reasonably satisfactory to Landlord that the value of Landlord's interest under this Lease shall not be diminished or reduced by the proposed Transfer. Such evidence shall include evidence respecting the relevant business experience and financial responsibility and status of the proposed transferee, assignee or sublessee;

(e) Tenant shall reimburse Landlord for Landlord's actual costs and expenses, including reasonable attorneys' fees, charges and disbursements incurred in connection with the review, processing and documentation of such request;

(f) Except with respect to an Exempt Transfer, if Tenant's transfer of rights or sharing of the Premises provides for the receipt by, on behalf of or on account of Tenant of any consideration of any kind whatsoever (including a premium rental for a sublease or lump sum payment for an assignment, but excluding Tenant's reasonable costs in marketing and subleasing the Premises) in excess of the rental and other charges due to Landlord under this Lease, Tenant shall pay fifty percent (50%) of all of such excess to Landlord, after making deductions for any

reasonable marketing expenses, tenant improvement funds expended by Tenant, alterations, cash concessions, brokerage commissions, attorneys' fees and free rent actually paid by Tenant. If such consideration consists of cash paid to Tenant, payment to Landlord shall be made upon receipt by Tenant of such cash payment;

(g) The proposed transferee, assignee or sublessee shall agree that, in the event Landlord gives such proposed transferee, assignee or sublessee notice that Tenant is in default under this Lease, such proposed transferee, assignee or sublessee shall thereafter make all payments otherwise due Tenant directly to Landlord, which payments shall be received by Landlord without any liability being incurred by Landlord, except to credit such payment against those due by Tenant under this Lease, and any such proposed transferee, assignee or sublessee shall agree to attorn to Landlord or its successors and assigns should this Lease be terminated for any reason; provided , however, that in no event shall Landlord or its Lenders, successors or assigns be obligated to accept such attornment;

(h) Landlord's consent to any such Transfer shall be effected on Landlord's commercially reasonable forms;

(i) Tenant shall not then be in Default hereunder in any respect;

(j) Such proposed transferee, assignee or sublessee's use of the Premises shall be the same as the Permitted Use;

(k) Landlord shall not be bound by any provision of any agreement pertaining to the Transfer, except for Landlord's written consent to the same;

(l) Tenant shall pay all transfer and other taxes (including interest and penalties) assessed or payable for any Transfer;

(m) Landlord's consent (or waiver of its rights) for any Transfer shall not waive Landlord's right to consent or refuse consent to any later Transfer;

(n) Tenant shall deliver to Landlord one executed copy of any and all written instruments evidencing or relating to the Transfer; and

(o) Tenant shall deliver to Landlord a list of Hazardous Materials (as defined below), certified by the proposed transferee, assignee or sublessee to be true and correct, that the proposed transferee, assignee or sublessee intends to use or store in the Premises. Additionally, Tenant shall deliver to Landlord, on or before the date any proposed transferee, assignee or sublessee takes occupancy of the Premises, all of the items relating to Hazardous Materials of such proposed transferee, assignee or sublessee as described in Section 21.2 .

29.5. Any Transfer that is not in compliance with the provisions of this Article or with respect to which Tenant does not fulfill its obligations pursuant to this Article shall be void and shall, at the option of Landlord, terminate this Lease.

29.6. Notwithstanding any Transfer, Tenant shall remain fully and primarily liable for the payment of all Rent and other sums due or to become due hereunder, and for the full performance of all other terms, conditions and covenants to be kept and performed by Tenant. The acceptance of Rent or any other sum due hereunder, or the acceptance of performance of any other term, covenant or condition thereof, from any person or entity other than Tenant shall not be deemed a waiver of any of the provisions of this Lease or a consent to any Transfer.

29.7. If Tenant delivers to Landlord a Transfer Notice indicating a desire to transfer this Lease to a proposed transferee, assignee or sublessee other than pursuant to an Exempt Transfer, then Landlord shall have the option, exercisable by giving notice to Tenant at any time within ten (10) business days after Landlord's receipt of such Transfer Notice, to terminate this Lease as of the date specified in the Transfer Notice as the Transfer Date, except for those provisions that, by their express terms, survive the expiration or earlier termination hereof. If Landlord exercises such option, then Tenant shall have the right to withdraw such Transfer Notice by delivering to Landlord written notice of such election within five (5) days after Landlord's delivery of notice electing to exercise Landlord's option to terminate this Lease. In the event Tenant withdraws the Transfer Notice as provided in this Section, this Lease shall continue in full force and effect. No failure of Landlord to exercise its option to terminate this Lease shall be deemed to be Landlord's consent to a proposed Transfer.

29.8. If Tenant sublets the Premises or any portion thereof, Tenant hereby immediately and irrevocably assigns to Landlord, as security for Tenant's obligations under this Lease, all rent from any such subletting, and appoints Landlord as assignee and attorney-in-fact for Tenant, and Landlord (or a receiver for Tenant appointed on Landlord's application) may collect such rent and apply it toward Tenant's obligations under this Lease; provided that, until the occurrence of a Default (as defined below) by Tenant, Tenant shall have the right to collect such rent.

29.9. In the event that Tenant enters into a sublease for the entire Premises in accordance with this Article that expires within two (2) days of the Term Expiration Date, the term expiration date of such sublease shall, notwithstanding anything in this Lease, the sublease or any consent to the sublease to the contrary, be deemed to be the date that is two (2) days prior to the Term Expiration Date.

30. Subordination and Attornment .

30.1. This Lease shall be subject and subordinate to the lien of any mortgage, deed of trust, or lease in which Landlord is tenant now or hereafter in force against the Building or the Project and to all advances made or hereafter to be made upon the security thereof without the necessity of the execution and delivery of any further instruments on the part of Tenant to effectuate such subordination.

30.2. Notwithstanding the foregoing, Tenant shall execute and deliver upon demand such further instrument or instruments evidencing such subordination of this Lease to the lien of any such mortgage or mortgages or deeds of trust or lease in which Landlord is tenant as may be required by Landlord; provided that such instrument(s) contain commercially reasonable non-disturbance language in favor of Tenant. If any Lender so elects, however, this Lease shall be

deemed prior in lien to any such lease, mortgage, or deed of trust upon or including the Premises regardless of date and Tenant shall execute a statement in writing to such effect at Landlord's request. If Tenant fails to execute any document required from Tenant under this Section within ten (10) days after written request therefor, Tenant hereby constitutes and appoints Landlord or its special attorney-in-fact to execute and deliver any such document or documents in the name of Tenant. Such power is coupled with an interest and is irrevocable. For the avoidance of doubt, "Lenders" shall also include historic tax credit investors and new market tax credit investors.

30.3. Upon written request of Landlord and opportunity for Tenant to review, Tenant agrees to execute any Lease amendments not materially altering the terms of this Lease, if required by a Lender incident to the financing of the real property of which the Premises constitute a part.

30.4. In the event any proceedings are brought for foreclosure, or in the event of the exercise of the power of sale under any mortgage or deed of trust made by Landlord covering the Premises, Tenant shall at the election of the purchaser at such foreclosure or sale attorn to the purchaser upon any such foreclosure or sale and recognize such purchaser as Landlord under this Lease.

31. Defaults and Remedies .

31.1. Late payment by Tenant to Landlord of Rent and other sums due shall cause Landlord to incur costs not contemplated by this Lease, the exact amount of which shall be extremely difficult and impracticable to ascertain. Such costs include processing and accounting charges and late charges that may be imposed on Landlord by the terms of any mortgage or trust deed covering the Premises. Therefore, if any installment of Rent due from Tenant is not received by Landlord within three (3) days after the date such payment is due, Tenant shall pay to Landlord (a) an additional sum of five percent (5%) of the overdue Rent as a late charge plus (b) interest at an annual rate (the " Default Rate ") equal to the lesser of (a) ten percent (10%) and (b) the highest rate permitted by Applicable Laws. The parties agree that this late charge represents a fair and reasonable estimate of the costs that Landlord shall incur by reason of late payment by Tenant and shall be payable as Additional Rent to Landlord due with the next installment of Rent or within five (5) business days after Landlord's demand, whichever is earlier. Landlord's acceptance of any Additional Rent (including a late charge or any other amount hereunder) shall not be deemed an extension of the date that Rent is due or prevent Landlord from pursuing any other rights or remedies under this Lease, at law or in equity. Notwithstanding anything to the contrary in this Section, Tenant shall not be obligated to pay a late charge pursuant to this Section for the first (1 st) late payment of Rent during any twelve (12) month period during the Term, unless Tenant fails to make such payment within five (5) days after Tenant's receipt of notice from Landlord regarding such late payment.

31.2. No payment by Tenant or receipt by Landlord of a lesser amount than the Rent payment herein stipulated shall be deemed to be other than on account of the Rent, nor shall any endorsement or statement on any check or any letter accompanying any check or payment as Rent be deemed an accord and satisfaction, and Landlord may accept such check or payment without prejudice to Landlord's right to recover the balance of such Rent or pursue any other

remedy provided in this Lease or in equity or at law. If a dispute shall arise as to any amount or sum of money to be paid by Tenant to Landlord hereunder, Tenant shall have the right to make payment "under protest," such payment shall not be regarded as a voluntary payment, and there shall survive the right on the part of Tenant to institute suit for recovery of the payment paid under protest.

31.3. If Tenant fails to pay any sum of money required to be paid by it hereunder or perform any other act on its part to be performed hereunder, in each case within the applicable cure period (if any) described in Section 31.4, then Landlord may (but shall not be obligated to), without waiving or releasing Tenant from any obligations of Tenant, make such payment or perform such act; provided that such failure by Tenant unreasonably interfered with the use of the Building or the Project by any other tenant or with the efficient operation of the Building or the Project, or resulted or could have resulted in a violation of Applicable Laws or the cancellation of an insurance policy maintained by Landlord. Notwithstanding the foregoing, in the event of an emergency, Landlord shall have the right to enter the Premises and act in accordance with its rights as provided elsewhere in this Lease. In addition to the late charge described in Section 31.1, Tenant shall pay to Landlord as Additional Rent all sums so paid or incurred by Landlord, together with interest at the Default Rate, computed from the date such sums were paid or incurred.

31.4. The occurrence of any one or more of the following events shall constitute a "Default" hereunder by Tenant:

(a) Tenant abandons the Premises;

(b) Tenant fails to make any payment of Rent, as and when due, or to satisfy its obligations under Article 19, where such failure shall continue for a period of three (3) days after written notice thereof from Landlord to Tenant;

(c) Tenant fails to observe or perform any obligation or covenant contained herein (other than described in Sections 31.4(a) and 31.4(b)) to be performed by Tenant, where such failure continues for a period of ten (10) days after written notice thereof from Landlord to Tenant; provided that, if the nature of Tenant's default is such that it reasonably requires more than ten (10) days to cure, Tenant shall not be deemed to be in Default if Tenant commences such cure within such ten (10) day period and thereafter diligently prosecutes the same to completion; and provided, further, that such cure is completed no later than sixty (60) days after Tenant's receipt of written notice from Landlord;

(d) Tenant makes an assignment for the benefit of creditors;

(e) A receiver, trustee or custodian is appointed to or does take title, possession or control of all or substantially all of Tenant's assets;

(f) Tenant files a voluntary petition under the United States Bankruptcy Code or any successor statute (as the same may be amended from time to time, the "Bankruptcy Code") or an order for relief is entered against Tenant pursuant to a voluntary or involuntary proceeding commenced under any chapter of the Bankruptcy Code;

(g) Any involuntary petition is filed against Tenant under any chapter of the Bankruptcy Code and is not dismissed within one hundred twenty (120) days;

(h) Tenant fails to deliver an estoppel certificate in accordance with Article 20 ; or

(i) Tenant's interest in this Lease is attached, executed upon or otherwise judicially seized and such action is not released within one hundred twenty (120) days of the action.

Notices given under this Section shall specify the alleged default and shall demand that Tenant perform the provisions of this Lease or pay the Rent that is in arrears, as the case may be, within the applicable period of time, or quit the Premises. No such notice shall be deemed a forfeiture or a termination of this Lease unless Landlord elects otherwise in such notice.

31.5. In the event of a Default by Tenant, and at any time thereafter, with or without notice or demand and without limiting Landlord in the exercise of any right or remedy that Landlord may have, Landlord has the right to do any or all of the following:

(a) Halt any Tenant Improvements and Alterations and order Tenant's contractors, subcontractors, consultants, designers and material suppliers to stop work;

(b) Terminate Tenant's right to possession of the Premises by written notice to Tenant or by any lawful means, in which case Tenant shall immediately surrender possession of the Premises to Landlord. In such event, Landlord shall have the immediate right to re-enter and remove all persons and property, and such property may be removed and stored in a public warehouse or elsewhere at the cost and for the account of Tenant, all without service of notice or resort to legal process and without being deemed guilty of trespass or becoming liable for any loss or damage that may be occasioned thereby; and

(c) Terminate this Lease, in which event Tenant shall immediately surrender possession of the Premises to Landlord. In such event, Landlord shall have the immediate right to re-enter and remove all persons and property, and such property may be removed and stored in a public warehouse or elsewhere at the cost and for the account of Tenant, all without service of notice or resort to legal process and without being deemed guilty of trespass or becoming liable for any loss or damage that may be occasioned thereby. In the event that Landlord shall elect to so terminate this Lease, then Landlord shall be entitled to recover from Tenant all damages incurred by Landlord by reason of Tenant's default, including:

(i) The sum of:

A. The worth at the time of award of any unpaid Rent that had accrued at the time of such termination; plus

B. The worth at the time of award of the amount by which the unpaid Rent that would have accrued during the period commencing with termination of the Lease and ending at the time of award exceeds that portion of the loss of Landlord's rental income from the Premises that Tenant proves to Landlord's reasonable satisfaction could have been reasonably avoided; plus

C. The worth at the time of award of the amount by which the unpaid Rent for the balance of the Term after the time of award exceeds that portion of the loss of Landlord's rental income from the Premises that Tenant proves to Landlord's reasonable satisfaction could have been reasonably avoided; plus

D. Any other amount necessary to compensate Landlord for all the detriment caused by Tenant's failure to perform its obligations under this Lease or that in the ordinary course of things would be likely to result therefrom, including the cost of restoring the Premises to the condition required under the terms of this Lease, including any rent payments not otherwise chargeable to Tenant (e.g., during any "free" rent period or rent holiday); plus

E. At Landlord's election, such other amounts in addition to or in lieu of the foregoing as may be permitted from time to time by Applicable Laws; or

(ii) At Landlord's election, as minimum liquidated damages in addition to any (A) amounts paid or payable to Landlord pursuant to Section 31.5(c)(i)(A) prior to such election and (B) costs of restoring the Premises to the condition required under the terms of this Lease, an amount (the " Election Amount ") equal to either (Y) the positive difference (if any, and measured at the time of such termination) between (1) the then-present value of the total Rent and other benefits that would have accrued to Landlord under this Lease for the remainder of the Term if Tenant had fully complied with the Lease minus (2) the then-present cash rental value of the Premises as determined by Landlord for what would be the then-unexpired Term if the Lease remained in effect, computed using the discount rate of the Federal Reserve Bank of San Francisco at the time of the award plus one (1) percentage point (the " Discount Rate ") or (Z) twelve (12) months (or such lesser number of months as may then be remaining in the Term) of Base Rent and Additional Rent at the rate last payable by Tenant pursuant to this Lease, in either case as Landlord specifies in such election. Landlord and Tenant agree that the Election Amount represents a reasonable forecast of the minimum damages expected to occur in the event of a breach, taking into account the uncertainty, time and cost of determining elements relevant to actual damages, such as fair market rent, time and costs that may be required to re-lease the Premises, and other factors; and that the Election Amount is not a penalty.

As used in Sections 31.5(c)(i)(A) and (B) , "worth at the time of award" shall be computed by allowing interest at the Default Rate. As used in Section 31.5(c)(i)(C) , the "worth at the time of the award" shall be computed by taking the present value of such amount, using the Discount Rate.

31.6. In addition to any other remedies available to Landlord at law or in equity and under this Lease, Landlord shall have the remedy described in California Civil Code Section 1951.4 and may continue this Lease in effect after Tenant's Default or abandonment and recover Rent as it becomes due, provided Tenant has the right to sublet or assign, subject only to reasonable limitations. In addition, Landlord shall not be liable in any way whatsoever for its

failure or refusal to relet the Premises. For purposes of this Section, the following acts by Landlord will not constitute the termination of Tenant's right to possession of the Premises:

(a) Acts of maintenance or preservation or efforts to relet the Premises, including alterations, remodeling, redecorating, repairs, replacements or painting as Landlord shall consider advisable for the purpose of reletting the Premises or any part thereof; or

(b) The appointment of a receiver upon the initiative of Landlord to protect Landlord's interest under this Lease or in the Premises.

Notwithstanding the foregoing, in the event of a Default by Tenant, Landlord may elect at any time to terminate this Lease and to recover damages to which Landlord is entitled.

31.7. If Landlord does not elect to terminate this Lease as provided in Section 31.5 , then Landlord may, from time to time, recover all Rent as it becomes due under this Lease. At any time thereafter, Landlord may elect to terminate this Lease and to recover damages to which Landlord is entitled.

31.8. In the event Landlord elects to terminate this Lease and relet the Premises, Landlord may execute any new lease in its own name. Tenant hereunder shall have no right or authority whatsoever to collect any Rent from such tenant. The proceeds of any such reletting shall be applied as follows:

(a) First, to the payment of any indebtedness other than Rent due hereunder from Tenant to Landlord, including storage charges or brokerage commissions owing from Tenant to Landlord as the result of such reletting;

(b) Second, to the payment of the costs and expenses of reletting the Premises, including (i) alterations and repairs that Landlord deems reasonably necessary and advisable and (ii) reasonable attorneys' fees, charges and disbursements incurred by Landlord in connection with the retaking of the Premises and such reletting;

(c) Third, to the payment of Rent and other charges due and unpaid hereunder; and

(d) Fourth, to the payment of future Rent and other damages payable by Tenant under this Lease.

31.9. All of Landlord's rights, options and remedies hereunder shall be construed and held to be nonexclusive and cumulative. Landlord shall have the right to pursue any one or all of such remedies, or any other remedy or relief that may be provided by Applicable Laws, whether or not stated in this Lease. No waiver of any default of Tenant hereunder shall be implied from any acceptance by Landlord of any Rent or other payments due hereunder or any omission by Landlord to take any action on account of such default if such default persists or is repeated, and no express waiver shall affect defaults other than as specified in such waiver. Notwithstanding any provision of this Lease to the contrary, in no event shall Landlord be required to mitigate its damages with respect to any default by Tenant, except as required by Applicable Laws. Any

such obligation imposed by Applicable Laws upon Landlord to relet the Premises after any termination of this Lease shall be subject to the reasonable requirements of Landlord to (a) lease to high quality tenants on such terms as Landlord may from time to time deem appropriate in its discretion and (b) develop the Project in a harmonious manner with a mix of uses, tenants, floor areas, terms of tenancies, etc., as determined by Landlord. Landlord shall not be obligated to relet the Premises to (y) any Tenant's Affiliate or (z) any party (i) unacceptable to a Lender, (ii) that requires Landlord to make improvements to or re-demise the Premises, (iii) that desires to change the Permitted Use, (iv) that desires to lease the Premises for more or less than the remaining Term or (v) to whom Landlord or an affiliate of Landlord may desire to lease other available space in the Project or at another property owned by Landlord or an affiliate of Landlord.

31.10. Landlord's termination of (a) this Lease or (b) Tenant's right to possession of the Premises shall not relieve Tenant of any liability to Landlord that has previously accrued or that shall arise based upon events that occurred prior to the later to occur of (y) the date of Lease termination and (z) the date Tenant surrenders possession of the Premises.

31.11. To the extent permitted by Applicable Laws, Tenant waives any and all rights of redemption granted by or under any present or future Applicable Laws if Tenant is evicted or dispossessed for any cause, or if Landlord obtains possession of the Premises due to Tenant's default hereunder or otherwise.

31.12. Landlord shall not be in default or liable for damages under this Lease unless Landlord fails to perform obligations required of Landlord within a reasonable time, but in no event shall such failure continue for more than thirty (30) days after written notice from Tenant specifying the nature of Landlord's failure; provided , however, that if the nature of Landlord's obligation is such that more than thirty (30) days are required for its performance, then Landlord shall not be in default if Landlord commences performance within such thirty (30) day period and thereafter diligently prosecutes the same to completion. In no event shall Tenant have the right to terminate or cancel this Lease or to withhold or abate rent or to set off any Claims against Rent as a result of any default or breach by Landlord of any of its covenants, obligations, representations, warranties or promises hereunder, except as may otherwise be expressly set forth in this Lease.

31.13. In the event of any default by Landlord, Tenant shall give notice by registered or certified mail to any (a) beneficiary of a deed of trust or (b) mortgagee under a mortgage covering the Premises, the Building or the Project and to any landlord of any lease of land upon or within which the Premises, the Building or the Project is located, and shall offer such beneficiary, mortgagee or landlord a reasonable opportunity to cure the default, including time to obtain possession of the Building or the Project by power of sale or a judicial action if such should prove necessary to effect a cure; provided that Landlord shall have furnished to Tenant in writing the names and addresses of all such persons who are to receive such notices.

32. Bankruptcy . In the event a debtor, trustee or debtor in possession under the Bankruptcy Code, or another person with similar rights, duties and powers under any other Applicable Laws, proposes to cure any default under this Lease or to assume or assign this Lease and is obliged to provide adequate assurance to Landlord that (a) a default shall be cured, (b) Landlord shall be

compensated for its damages arising from any breach of this Lease and (c) future performance of Tenant's obligations under this Lease shall occur, then such adequate assurances shall include any or all of the following, as designated by Landlord in its sole and absolute discretion:

32.1. Those acts specified in the Bankruptcy Code or other Applicable Laws as included within the meaning of "adequate assurance," even if this Lease does not concern a shopping center or other facility described in such Applicable Laws;

32.2. A prompt cash payment to compensate Landlord for any monetary defaults or actual damages arising directly from a breach of this Lease;

32.3. A cash deposit in an amount at least equal to the then-current amount of the Security Deposit; or

32.4. The assumption or assignment of all of Tenant's interest and obligations under this Lease.

33. Brokers .

33.1. Tenant represents and warrants that it has had no dealings with any real estate broker or agent in connection with the negotiation of this Lease other than Newmark Cornish and Carey (" Broker "), and that it knows of no other real estate broker or agent that is or might be entitled to a commission in connection with this Lease. Landlord represents and warrants that it has had no dealings with any real estate broker or agent in connection with the negotiation of this Lease other than Kidder Mathews, and that it knows of no other real estate broker or agent that is or might be entitled to a commission in connection with this Lease. Landlord shall compensate Broker in relation to this Lease pursuant to a separate agreement between Landlord and Broker.

33.2. Tenant represents and warrants that no broker or agent has made any representation or warranty relied upon by Tenant in Tenant's decision to enter into this Lease, other than as contained in this Lease.

33.3. Tenant acknowledges and agrees that the employment of brokers by Landlord is for the purpose of solicitation of offers of leases from prospective tenants and that no authority is granted to any broker to furnish any representation (written or oral) or warranty from Landlord unless expressly contained within this Lease. Landlord is executing this Lease in reliance upon Tenant's representations, warranties and agreements contained within Sections 33.1 and 33.2 .

33.4. Tenant agrees to Indemnify the Landlord Indemnitees from any and all cost or liability for compensation claimed by any broker or agent, other than Broker, employed or engaged by Tenant or claiming to have been employed or engaged by Tenant.

34. Definition of Landlord . With regard to obligations imposed upon Landlord pursuant to this Lease, the term " Landlord ," as used in this Lease, shall refer only to Landlord or Landlord's then-current successor-in-interest. In the event of any transfer, assignment or conveyance of Landlord's interest in this Lease or in Landlord's fee title to or leasehold interest in the Property, as applicable, Landlord herein named (and in case of any subsequent transfers or conveyances, the subsequent Landlord) shall be automatically freed and relieved, from and after the date of

such transfer, assignment or conveyance, from all liability for the performance of any covenants or obligations contained in this Lease thereafter to be performed by Landlord and, without further agreement, the transferee, assignee or conveyee of Landlord's in this Lease or in Landlord's fee title to or leasehold interest in the Property, as applicable, shall be deemed to have assumed and agreed to observe and perform any and all covenants and obligations of Landlord hereunder during the tenure of its interest in the Lease or the Property. Landlord or any subsequent Landlord may transfer its interest in the Premises or this Lease without Tenant's consent.

35. Limitation of Landlord ' s Liability .

35.1. If Landlord is in default under this Lease and, as a consequence, Tenant recovers a monetary judgment against Landlord, the judgment shall be satisfied only out of (a) the proceeds of sale received on execution of the judgment and levy against the right, title and interest of Landlord in the Building and the Project, (b) rent or other income from such real property receivable by Landlord or (c) the consideration received by Landlord from the sale, financing, refinancing or other disposition of all or any part of Landlord's right, title or interest in the Building or the Project.

35.2. Neither Landlord nor any of its affiliates, nor any of their respective partners, shareholders, directors, officers, employees, members or agents shall be personally liable for Landlord's obligations or any deficiency under this Lease, and service of process shall not be made against any shareholder, director, officer, employee or agent of Landlord or any of Landlord's affiliates. No partner, shareholder, director, officer, employee, member or agent of Landlord or any of its affiliates shall be sued or named as a party in any suit or action, and service of process shall not be made against any partner or member of Landlord except as may be necessary to secure jurisdiction of the partnership, joint venture or limited liability company, as applicable. No partner, shareholder, director, officer, employee, member or agent of Landlord or any of its affiliates shall be required to answer or otherwise plead to any service of process, and no judgment shall be taken or writ of execution levied against any partner, shareholder, director, officer, employee, member or agent of Landlord or any of its affiliates.

35.3. Each of the covenants and agreements of this Article shall be applicable to any covenant or agreement either expressly contained in this Lease or imposed by Applicable Laws and shall survive the expiration or earlier termination of this Lease.

36. Joint and Several Obligations . If more than one person or entity executes this Lease as Tenant, then:

36.1. Each of them is jointly and severally liable for the keeping, observing and performing of all of the terms, covenants, conditions, provisions and agreements of this Lease to be kept, observed or performed by Tenant, and such terms, covenants, conditions, provisions and agreements shall be binding with the same force and effect upon each and all of the persons executing this Agreement as Tenant; and

36.2. The term " Tenant ," as used in this Lease, shall mean and include each of them, jointly and severally. The act of, notice from, notice to, refund to, or signature of any one or

more of them with respect to the tenancy under this Lease, including any renewal, extension, expiration, termination or modification of this Lease, shall be binding upon each and all of the persons executing this Lease as Tenant with the same force and effect as if each and all of them had so acted, so given or received such notice or refund, or so signed.

37. Representations . Tenant guarantees, warrants and represents that (a) Tenant is duly incorporated or otherwise established or formed and validly existing under the laws of its state of incorporation, establishment or formation, (b) Tenant has and is duly qualified to do business in the state in which the Property is located, (c) Tenant has full corporate, partnership, trust, association or other appropriate power and authority to enter into this Lease and to perform all Tenant's obligations hereunder, (d) each person (and all of the persons if more than one signs) signing this Lease on behalf of Tenant is duly and validly authorized to do so and (e) neither (i) the execution, delivery or performance of this Lease nor (ii) the consummation of the transactions contemplated hereby will violate or conflict with any provision of documents or instruments under which Tenant is constituted or to which Tenant is a party. In addition, Tenant guarantees, warrants and represents that none of (x) it, (y) its affiliates or partners nor (z) to the best of its knowledge, its members, shareholders or other equity owners or any of their respective employees, officers, directors, representatives or agents is a person or entity with whom U.S. persons or entities are restricted from doing business under regulations of the Office of Foreign Asset Control (" OFAC ") of the Department of the Treasury (including those named on OFAC's Specially Designated and Blocked Persons List) or under any statute, executive order (including the September 24, 2001, Executive Order Blocking Property and Prohibiting Transactions with Persons Who Commit, Threaten to Commit, or Support Terrorism) or other similar governmental action.

38. Confidentiality . Tenant shall keep the terms and conditions of this Lease and any information provided to Tenant or its employees, agents or contractors pursuant to Article 9 confidential and shall not (a) disclose to any third party any terms or conditions of this Lease or any other Lease-related document (including subleases, assignments, work letters, construction contracts, letters of credit, subordination agreements, non-disturbance agreements, brokerage agreements or estoppels) or (b) provide to any third party an original or copy of this Lease (or any Lease-related document). Landlord shall not release to any third party any non-public financial information or non-public information about Tenant's ownership structure that Tenant gives Landlord. Notwithstanding the foregoing, confidential information under this Section may be released by Landlord or Tenant under the following circumstances: (x) if required by Applicable Laws (including, without limitation, any applicable rules and regulations established by the United States Securities and Exchange Commission) or in any judicial proceeding; provided that the releasing party has given the other party reasonable notice of such requirement, if feasible, (y) to a party's attorneys, accountants, brokers, lenders, potential lenders, investors, potential investors and other bona fide consultants or advisers (with respect to this Lease only); provided such third parties agree to be bound by this Section or (z) to bona fide prospective assignees or subtenants of this Lease; provided they agree in writing to be bound by this Section.

39. Notices . Except as otherwise stated in this Lease, any notice, consent, demand, invoice, statement or other communication required or permitted to be given hereunder shall be in writing and shall be given by (a) personal delivery, (b) overnight delivery with a reputable international

overnight delivery service, such as FedEx, or (c) facsimile or email transmission, so long as such transmission is followed within one (1) business day by delivery utilizing one of the methods described in Subsection 39(a) or (b) . Any such notice, consent, demand, invoice, statement or other communication shall be deemed delivered (x) upon receipt, if given in accordance with Subsection 39(a) ; (y) one (1) business day after deposit with a reputable international overnight delivery service, if given if given in accordance with Subsection 39(b) ; or (z) upon transmission, if given in accordance with Subsection 39(c) . Except as otherwise stated in this Lease, any notice, consent, demand, invoice, statement or other communication required or permitted to be given pursuant to this Lease shall be addressed to Tenant at the Premises, or to Landlord or Tenant at the addresses shown in Sections 2.9 and 2.10 or 2.11 , respectively. Either party may, by notice to the other given pursuant to this Section, specify additional or different addresses for notice purposes.

40. Miscellaneous .

40.1. Landlord reserves the right to change the name of the Building or the Project in its sole discretion.

40.2. To induce Landlord to enter into this Lease, Tenant agrees that it shall furnish to Landlord, from time to time, within ten (10) business days after receipt of Landlord's written request, the most recent year-end unconsolidated financial statements reflecting Tenant's current financial condition audited by a nationally recognized accounting firm. Tenant shall, within ninety (90) days after the end of Tenant's financial year, furnish Landlord with a certified copy of Tenant's year-end unconsolidated financial statements for the previous year audited by a nationally recognized accounting firm. Tenant represents and warrants that all financial statements, records and information furnished by Tenant to Landlord in connection with this Lease are true, correct and complete in all respects. If audited financials are not otherwise prepared, unaudited financials complying with generally accepted accounting principles and certified by the chief financial officer of Tenant as true, correct and complete in all respects shall suffice for purposes of this Section. The provisions of this Section shall not apply at any time while Tenant is a corporation whose shares are traded on any nationally recognized stock exchange.

40.3. Submission of this instrument for examination or signature by Tenant does not constitute a reservation of or option for a lease, and shall not be effective as a lease or otherwise until execution by and delivery to both Landlord and Tenant.

40.4. The terms of this Lease are intended by the parties as a final, complete and exclusive expression of their agreement with respect to the terms that are included herein, and may not be contradicted or supplemented by evidence of any other prior or contemporaneous agreement.

40.5. Landlord may, but shall not be obligated to, record a short form or memorandum hereof without Tenant's consent. Within ten (10) days after receipt of written request from Landlord, Tenant shall execute a termination of any short form or memorandum of lease recorded with respect hereto. Tenant shall be responsible for the cost of recording any short form or memorandum of this Lease, including any transfer or other taxes incurred in connection with such recordation. Neither party shall record this Lease.

40.6. Where applicable in this Lease, the singular includes the plural and the masculine or neuter includes the masculine, feminine and neuter. The words "include," "includes," "included" and "including" mean "'include,' etc., without limitation." The word "shall" is mandatory and the word "may" is permissive. The section headings of this Lease are not a part of this Lease and shall have no effect upon the construction or interpretation of any part of this Lease. Landlord and Tenant have each participated in the drafting and negotiation of this Lease, and the language in all parts of this Lease shall be in all cases construed as a whole according to its fair meaning and not strictly for or against either Landlord or Tenant.

40.7. Except as otherwise expressly set forth in this Lease, each party shall pay its own costs and expenses incurred in connection with this Lease and such party's performance under this Lease; provided that, if either party commences an action, proceeding, demand, claim, action, cause of action or suit against the other party arising out of or in connection with this Lease, then the substantially prevailing party shall be reimbursed by the other party for all reasonable costs and expenses, including reasonable attorneys' fees and expenses, incurred by the substantially prevailing party in such action, proceeding, demand, claim, action, cause of action or suit, and in any appeal in connection therewith (regardless of whether the applicable action, proceeding, demand, claim, action, cause of action, suit or appeal is voluntarily withdrawn or dismissed). In addition, Landlord shall, upon demand, be entitled to all reasonable attorneys' fees and all other reasonable costs incurred in the preparation and service of any notice or demand hereunder, regardless of whether a legal action is subsequently commenced, or incurred in connection with any contested matter or other proceeding in bankruptcy court concerning this Lease.

40.8. Time is of the essence with respect to the performance of every provision of this Lease.

40.9. Each provision of this Lease performable by Tenant shall be deemed both a covenant and a condition.

40.10. Notwithstanding anything to the contrary contained in this Lease, Tenant's obligations under this Lease are independent and shall not be conditioned upon performance by Landlord.

40.11. Whenever consent or approval of either party is required, that party shall not unreasonably withhold, condition or delay such consent or approval, except as may be expressly set forth to the contrary.

40.12. Any provision of this Lease that shall prove to be invalid, void or illegal shall in no way affect, impair or invalidate any other provision hereof, and all other provisions of this Lease shall remain in full force and effect and shall be interpreted as if the invalid, void or illegal provision did not exist.

40.13. Each of the covenants, conditions and agreements herein contained shall inure to the benefit of and shall apply to and be binding upon the parties hereto and their respective heirs; legatees; devisees; executors; administrators; and permitted successors and assigns. This Lease is for the sole benefit of the parties and their respective heirs, legatees, devisees, executors, administrators and permitted successors and assigns, and nothing in this Lease shall give or be construed to give any other person or entity any legal or equitable rights. Nothing in this Section shall in any way alter the provisions of this Lease restricting assignment or subletting.

40.14. This Lease shall be governed by, construed and enforced in accordance with the laws of the state in which the Premises are located, without regard to such state's conflict of law principles.

40.15. Tenant guarantees, warrants and represents that the individual or individuals signing this Lease have the power, authority and legal capacity to sign this Lease on behalf of and to bind all entities, corporations, partnerships, limited liability companies, joint venturers or other organizations and entities on whose behalf such individual or individuals have signed.

40.16. This Lease may be executed in one or more counterparts, each of which, when taken together, shall constitute one and the same document.

40.17. No provision of this Lease may be modified, amended or supplemented except by an agreement in writing signed by Landlord and Tenant.

40.18. No waiver of any term, covenant or condition of this Lease shall be binding upon Landlord unless executed in writing by Landlord. The waiver by Landlord of any breach or default of any term, covenant or condition contained in this Lease shall not be deemed to be a waiver of any preceding or subsequent breach or default of such term, covenant or condition or any other term, covenant or condition of this Lease.

40.19. To the extent permitted by Applicable Laws, the parties waive trial by jury in any action, proceeding or counterclaim brought by the other party hereto related to matters arising out of or in any way connected with this Lease; the relationship between Landlord and Tenant; Tenant's use or occupancy of the Premises; or any claim of injury or damage related to this Lease or the Premises.

40.20. Throughout the Term, Tenant shall have the right to use the furniture, fixtures and equipment currently located within the Premises and listed on Exhibit D attached hereto (collectively, the " FF&E "). Landlord has made no representations or warranties, express, implied or otherwise, regarding the condition or working order of the FF&E. Tenant confirms that it has had the reasonable opportunity to inventory and inspect the FF&E and hereby represents that (i) it accepts the FF&E " **AS IS AND WITH ALL FAULTS** ", and (ii) it is satisfied that all items of FF&E listed on Exhibit D attached hereto are currently located within the Premises and are hereby accepted by Tenant, subject to and in accordance with the terms of this Section. Tenant acknowledges and agrees that Landlord shall continue to own the FF&E, and Tenant shall acquire no ownership interest therein. Throughout the Term, Tenant shall be obligated to (a) maintain, repair, safeguard and keep lien free the FF&E, and (b) ensure that the FF&E is covered by the insurance policy required to be maintained by Tenant pursuant to

Section 23.3(c) of this Lease. With the exception of ordinary wear and tear, Tenant shall promptly repair or replace any FF&E that becomes damaged, destroyed or for any reason is no longer located at the Premises, and shall keep a detailed log of any such repairs or replacements. All replacements shall be of substantially similar style and quality as the original items of FF&E so replaced. Tenant shall provide Landlord with a copy of such log upon request. In no event shall Landlord have any liability or responsibility with respect to the FF&E, and Landlord shall have no responsibility to repair or refurbish the FF&E at any time. At the expiration or earlier termination of the Term, Landlord and Tenant shall jointly inventory the FF&E then located within the Premises, and Tenant shall pay to Landlord, within thirty (30) days following the effective date of expiration or earlier termination of this Lease, an amount equal to the cost to repair or replace any items of the FF&E which are no longer located at the Premises, are of inferior style or quality as compared with the original FF&E, or which exhibit damage beyond ordinary wear and tear as reasonably determined by Landlord.

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IN WITNESS WHEREOF, the parties hereto have executed this Lease as of the date first above written.

LANDLORD :

BMR-PACIFIC RESEARCH CENTER LP,
a Delaware limited partnership

By: _____
Name: _____
Title: _____

TENANT :

PROTAGONIST THERAPEUTICS, INC.,
a Delaware corporation

By: _____
Name: _____
Title: _____

EXHIBIT A

PREMISES

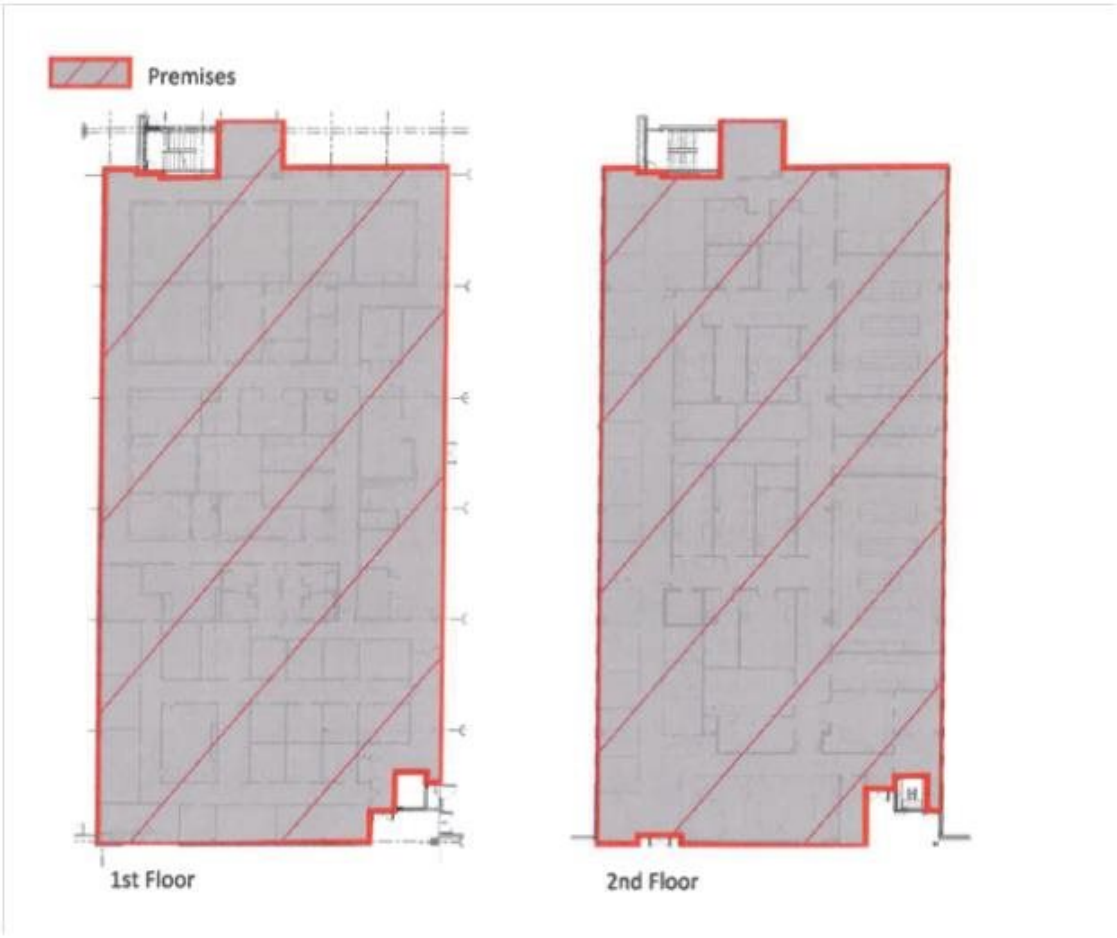

EXHIBIT B

WORK LETTER

This Work Letter (this " Work Letter ") is made and entered into as of the day of March, 2017, by and between BMR-PACIFIC RESEARCH CENTER LP, a Delaware limited partnership (" Landlord "), and PROTAGONIST THERAPEUTICS, INC., a Delaware corporation (" Tenant "), and is attached to and made a part of that certain Lease dated as of March , 2017 (as the same may be amended, amended and restated, supplemented or otherwise modified from time to time, the " Lease "), by and between Landlord and Tenant for the Premises located at 7707 Gateway Boulevard, Newark, California. All capitalized terms used but not otherwise defined herein shall have the meanings given them in the Lease.

1. General Requirements .

1.1. Authorized Representatives .

(a) Landlord designates, as Landlord's authorized representative (" Landlord's Authorized Representative "), (i) Ben Evans as the person authorized to initial plans, drawings, approvals and to sign change orders pursuant to this Work Letter and (ii) an officer of Landlord as the person authorized to sign any amendments to this Work Letter or the Lease. Tenant shall not be obligated to respond to or act upon any such item until such item has been initialed or signed (as applicable) by the appropriate Landlord's Authorized Representative. Landlord may change either Landlord's Authorized Representative upon one (1) business day's prior written notice to Tenant.

(b) Tenant designates Tom O'Neil (" Tenant's Authorized Representative ") as the person authorized to initial and sign all plans, drawings, change orders and approvals pursuant to this Work Letter. Landlord shall not be obligated to respond to or act upon any such item until such item has been initialed or signed (as applicable) by Tenant's Authorized Representative. Tenant may change Tenant's Authorized Representative upon one (1) business day's prior written notice to Landlord.

1.2. Schedule . The schedule for design and development of the Tenant Improvements, including the time periods for preparation and review of construction documents, approvals and performance, shall be in accordance with a schedule to be prepared by Tenant (the " Schedule "). Tenant shall prepare the Schedule so that it is a reasonable schedule for the completion of the Tenant Improvements. The Schedule shall clearly identify all activities requiring Landlord participation, including specific dates and time periods when Tenant's contractor will require access to areas of the Project outside of the Premises. As soon as the Schedule is completed, Tenant shall deliver the same to Landlord for Landlord's approval, which approval shall not be unreasonably withheld, conditioned or delayed. Such Schedule shall be approved or disapproved by Landlord within ten (10) business days after delivery to Landlord. Landlord's failure to respond within such ten (10) business day period shall be deemed approval by Landlord. If Landlord disapproves the Schedule, then Landlord shall notify Tenant in writing of its objections to such Schedule, and the parties shall confer and negotiate in good faith to reach agreement on the Schedule. The Schedule shall be subject to adjustment as mutually agreed upon in writing by the parties, or as provided in this Work Letter.

1.3. Tenant's Architects, Contractors and Consultants . The architect, engineering consultants, design team, general contractor and subcontractors responsible for the construction of the Tenant Improvements shall be selected by Tenant and approved by Landlord, which approval Landlord shall not unreasonably withhold, condition or delay. Landlord may refuse to use any architects, consultants, contractors, subcontractors or material suppliers that Landlord reasonably believes could cause labor disharmony or may not have sufficient experience, in Landlord's reasonable opinion, to perform work in an occupied Class "A" laboratory research building and in lab areas. All Tenant contracts related to the Tenant Improvements shall provide that Tenant may assign such contracts and any warranties with respect to the Tenant Improvements to Landlord at any time.

2. Tenant Improvements . All Tenant Improvements shall be performed by Tenant's contractor, at Tenant's sole cost and expense (subject to Landlord's obligations with respect to any portion of the TI Allowance) and in accordance with the Approved Plans (as defined below), the Lease and this Work Letter. To the extent that the total projected cost of the Tenant Improvements (as reasonably projected by Landlord) exceeds the TI Allowance (such excess, the " Excess TI Costs "), Tenant shall advance to Landlord any Excess TI Costs within ten (10) days after receipt of an invoice therefor, but in any case before Tenant commences the Tenant Improvements. If the actual Excess TI Costs are less than the Excess TI Costs paid by Tenant to Landlord, Landlord shall credit Tenant with the overage paid by Tenant against Tenant's Rent obligations, beginning after Landlord has completed the final accounting for the Tenant Improvements (which final accounting shall be completed within thirty (30) days following the completion of the Tenant Improvements). If the cost of the Tenant Improvements (as reasonably projected by Landlord) increases over Landlord's initial projection, then Landlord may notify Tenant and Tenant shall deposit any additional Excess TI Costs with Landlord in the same way that Tenant deposited the initial Excess TI Costs. If Tenant fails to pay, or is late in paying, any sum due to Landlord under this Work Letter (and Tenant fails to cure such non-payment within three (3) business days after notice from Landlord), then Landlord shall have all of the rights and remedies set forth in the Lease for nonpayment of Rent (including the right to interest and the right to assess a late charge), and for purposes of any litigation instituted with regard to such amounts the same shall be considered Rent. All material and equipment furnished by Tenant or its contractors as the Tenant Improvements shall be new or "like new;" the Tenant Improvements shall be performed in a first-class, workmanlike manner; and the quality of the Tenant Improvements shall be of a nature and character not less than the Building Standard. Tenant shall take, and shall require its contractors to take, commercially reasonable steps to protect the Premises during the performance of any Tenant Improvements, including covering or temporarily removing any window coverings so as to guard against dust, debris or damage. All Tenant Improvements shall be performed in accordance with Article 17 of the Lease; provided that, notwithstanding anything in the Lease or this Work Letter to the contrary, in the event of a conflict between this Work Letter and Article 17 of the Lease, the terms of this Work Letter shall govern.

2.1. Work Plans . Tenant shall prepare and submit to Landlord for approval schematics covering the Tenant Improvements prepared in conformity with the applicable provisions of this Work Letter (the " Draft Schematic Plans "). The Draft Schematic Plans shall contain sufficient information and detail to accurately describe the proposed design to Landlord and such other information as Landlord may reasonably request. Landlord shall notify Tenant in writing within ten (10) business days after receipt of the Draft Schematic Plans whether Landlord approves or objects to the Draft Schematic Plans and of the manner, if any, in which the Draft Schematic Plans are unacceptable. Landlord's failure to respond within such ten (10) business day period shall be deemed approval by Landlord. If Landlord reasonably objects to the Draft Schematic Plans, then Tenant shall revise the Draft Schematic Plans and cause Landlord's objections to be remedied in the revised Draft Schematic Plans. Tenant shall then resubmit the revised Draft Schematic Plans to Landlord for approval, such approval not to be unreasonably withheld, conditioned or delayed. Landlord's approval of or objection to revised Draft Schematic Plans and Tenant's correction of the same shall be in accordance with this Section until Landlord has approved the Draft Schematic Plans in writing or been deemed to have approved them. The iteration of the Draft Schematic Plans that is approved or deemed approved by Landlord without objection shall be referred to herein as the " Approved Schematic Plans ."

2.2. Construction Plans . Tenant shall prepare final plans and specifications for the Tenant Improvements that (a) are consistent with and are logical evolutions of the Approved Schematic Plans and (b) incorporate any other Tenant-requested (and Landlord-approved) Changes (as defined below). As soon as such final plans and specifications (" Construction Plans ") are completed, Tenant shall deliver the same to Landlord for Landlord's approval, which approval shall not be unreasonably withheld, conditioned or delayed. All such Construction Plans shall be submitted by Tenant to Landlord in electronic .pdf, CADD and full-size hard copy formats, and shall be approved or disapproved by Landlord within ten (10) business days after delivery to Landlord. Landlord's failure to respond within such ten (10) business day period shall be deemed approval by Landlord. If the Construction Plans are disapproved by Landlord, then Landlord shall notify Tenant in writing of its objections to such Construction Plans, and the parties shall confer and negotiate in good faith to reach agreement on the Construction Plans. Promptly after the Construction Plans are approved by Landlord and Tenant, two (2) copies of such Construction Plans shall be initialed and dated by Landlord and Tenant, and Tenant shall promptly submit such Construction Plans to all appropriate Governmental Authorities for approval. The Construction Plans so approved, and all change orders specifically permitted by this Work Letter, are referred to herein as the " Approved Plans ."

2.3. Changes to the Tenant Improvements . Any changes to the Approved Plans (each, a " Change ") shall be requested and instituted in accordance with the provisions of this Article 2 and shall be subject to the written approval of the non-requesting party in accordance with this Work Letter.

(a) Change Request . Either Landlord or Tenant may request Changes after Landlord approves the Approved Plans by notifying the other party thereof in writing in substantially the same form as the AIA standard change order form (a " Change Request "), which Change Request shall detail the nature and extent of any requested Changes, including (a) the

Change, (b) the party required to perform the Change and (c) any modification of the Approved Plans and the Schedule, as applicable, necessitated by the Change. If the nature of a Change requires revisions to the Approved Plans, then the requesting party shall be solely responsible for the cost and expense of such revisions and any increases in the cost of the Tenant Improvements as a result of such Change. Change Requests shall be signed by the requesting party's Authorized Representative.

(b) Approval of Changes . All Change Requests shall be subject to the other party's prior written approval, which approval shall not be unreasonably withheld, conditioned or delayed. The non-requesting party shall have three (3) business days after receipt of a Change Request to notify the requesting party in writing of the non-requesting party's decision either to approve or object to the Change Request. The non-requesting party's failure to respond within such three (3) business day period shall be deemed approval by the non-requesting party.

2.4. Preparation of Estimates . Tenant shall, before proceeding with any Change, using its best efforts, prepare as soon as is reasonably practicable (but in no event more than five (5) business days after delivering a Change Request to Landlord or receipt of a Change Request) an estimate of the increased costs or savings that would result from such Change, as well as an estimate of such Change's effects on the Schedule. Landlord shall have five (5) business days after receipt of such information from Tenant to (a) in the case of a Tenant-initiated Change Request, approve or reject such Change Request in writing, or (b) in the case of a Landlord-initiated Change Request, notify Tenant in writing of Landlord's decision either to proceed with or abandon the Landlord-initiated Change Request.

2.5. Quality Control Program; Coordination . Tenant shall provide Landlord with information regarding the following (together, the " QCP "): (a) Tenant's general contractor's quality control program and (b) evidence of subsequent monitoring and action plans. The QCP shall be subject to Landlord's reasonable review and approval and shall specifically address the Tenant Improvements. Tenant shall ensure that the QCP is regularly implemented on a scheduled basis and shall provide Landlord with reasonable prior notice and access to attend all inspections and meetings between Tenant and its general contractor. At the conclusion of the Tenant Improvements, Tenant shall deliver the quality control log to Landlord, which shall include all records of quality control meetings and testing and of inspections held in the field, including inspections relating to concrete, steel roofing, piping pressure testing and system commissioning.

3. Completion of Tenant Improvements . Tenant, at its sole cost and expense (except for the TI Allowance), shall perform and complete the Tenant Improvements in all respects (a) in substantial conformance with the Approved Plans, (b) otherwise in compliance with provisions of the Lease and this Work Letter and (c) in accordance with Applicable Laws, the requirements of Tenant's insurance carriers, the requirements of Landlord's insurance carriers (to the extent Landlord provides its insurance carriers' requirements to Tenant) and the board of fire underwriters having jurisdiction over the Premises. The Tenant Improvements shall be deemed completed at such time as Tenant shall furnish to Landlord (t) evidence satisfactory to Landlord that (i) all Tenant Improvements have been completed and paid for in full (which shall be evidenced by the architect's certificate of completion and the general contractor's and each

subcontractor's and material supplier's final unconditional waivers and releases of liens, each in a form acceptable to Landlord in its reasonable discretion and complying with Applicable Laws, and a Certificate of Substantial Completion in the form of the American Institute of Architects document G704, executed by the project architect and the general contractor, together with a statutory notice of substantial completion from the general contractor), (ii) all Tenant Improvements have been accepted by Landlord, (iii) any and all liens related to the Tenant Improvements have either been discharged of record (by payment, bond, order of a court of competent jurisdiction or otherwise) or waived by the party filing such lien and (iv) no security interests relating to the Tenant Improvements are outstanding, (u) all certifications and approvals with respect to the Tenant Improvements that may be required from any Governmental Authority and any board of fire underwriters or similar body for the use and occupancy of the Premises (including a certificate of occupancy (or its substantial equivalent) for the Premises for the Permitted Use), (v) certificates of insurance required by the Lease to be purchased and maintained by Tenant, (w) an affidavit from Tenant's architect certifying that all work performed in, on or about the Premises is in accordance with the Approved Plans, (x) complete "as built" drawing print sets, project specifications and shop drawings and electronic CADD files on disc (showing the Tenant Improvements as an overlay on the Building "as built" plans (provided that Landlord provides the Building "as-built" plans provided to Tenant) of all contract documents for work performed by their architect and engineers in relation to the Tenant Improvements, (y) a commissioning report prepared by a licensed, qualified commissioning agent hired by Tenant and approved by Landlord for all new or affected mechanical, electrical and plumbing systems (which report Landlord may hire a licensed, qualified commissioning agent to peer review, and whose reasonable recommendations Tenant's commissioning agent shall perform and incorporate into a revised report) and (z) such other "close out" materials as Landlord reasonably requests consistent with Landlord's own requirements for its contractors, such as copies of manufacturers' warranties, operation and maintenance manuals and the like.

4. Insurance .

4.1. Property Insurance . At all times during the period beginning with commencement of construction of the Tenant Improvements and ending with final completion of the Tenant Improvements, Tenant shall maintain, or cause to be maintained (in addition to the insurance required of Tenant pursuant to the Lease), property insurance insuring Landlord and the Landlord Parties, as their interests may appear. Such policy shall, on a completed values basis for the full insurable value at all times, insure against loss or damage by fire, vandalism and malicious mischief and other such risks as are customarily covered by the so-called "broad form extended coverage endorsement" upon all Tenant Improvements and the general contractor's and any subcontractors' machinery, tools and equipment, all while each forms a part of, or is contained in, the Tenant Improvements or any temporary structures on the Premises, or is adjacent thereto; provided that, for the avoidance of doubt, insurance coverage with respect to the general contractor's and any subcontractors' machinery, tools and equipment shall be carried on a primary basis by such general contractor or the applicable subcontractor(s). Tenant agrees to pay any deductible, and Landlord is not responsible for any deductible, for a claim under such insurance. Such property insurance shall contain an express waiver of any right of subrogation by the insurer against Landlord and the Landlord Parties, and shall name Landlord and its affiliates as loss payees as their interests may appear.

4.2. Workers' Compensation Insurance . At all times during the period of construction of the Tenant Improvements, Tenant shall, or shall cause its contractors or subcontractors to, maintain statutory workers' compensation insurance as required by Applicable Laws.

5. Liability . Tenant assumes sole responsibility and liability for any and all injuries or the death of any persons, including Tenant's contractors and subcontractors and their respective employees, agents and invitees, and for any and all damages to property caused by, resulting from or arising out of any act or omission on the part of Tenant, Tenant's contractors or subcontractors, or their respective employees, agents and invitees in the prosecution of the Tenant Improvements. Tenant agrees to Indemnify the Landlord Indemnitees from and against all Claims due to, because of or arising out of any and all such injuries, death or damage, whether real or alleged, and Tenant and Tenant's contractors and subcontractors shall assume and defend at their sole cost and expense all such Claims; provided , however , that nothing contained in this Work Letter shall be deemed to Indemnify Landlord from or against liability caused by Landlord's negligence or willful misconduct. Any deficiency in design or construction of the Tenant Improvements shall be solely the responsibility of Tenant, notwithstanding the fact that Landlord may have approved of the same in writing.

6. TI Allowance .

6.1. Application of TI Allowance . Landlord shall contribute the TI Allowance and any Excess TI Costs advanced by Tenant to Landlord toward the costs and expenses incurred in connection with the performance of the Tenant Improvements, in accordance with Article 4 of the Lease. If the entire TI Allowance is not applied toward or reserved for the costs of the Tenant Improvements on or before the deadline set forth in Section 4.3 of the Lease, then Tenant shall not be entitled to a credit of such unused portion of the TI Allowance. If the entire Excess TI Costs advanced by Tenant to Landlord are not applied toward the costs of the Tenant Improvements, then Landlord shall promptly return such excess to Tenant following completion of the Tenant Improvements. Tenant may apply the TI Allowance for the payment of construction and other costs in accordance with the terms and provisions of the Lease.

6.2. Approval of Budget for the Tenant Improvements . Notwithstanding anything to the contrary set forth elsewhere in this Work Letter or the Lease, Landlord shall not have any obligation to expend any portion of the TI Allowance until Landlord and Tenant shall have approved in writing the budget for the Tenant Improvements (the " Approved Budget "). Prior to Landlord's approval of the Approved Budget, Tenant shall pay all of the costs and expenses incurred in connection with the Tenant Improvements as they become due. Landlord shall not be obligated to reimburse Tenant for costs or expenses relating to the Tenant Improvements that exceed the amount of the TI Allowance. Landlord shall not unreasonably withhold, condition or delay its approval of any budget for Tenant Improvements that is proposed by Tenant.

6.3. Fund Requests . Upon submission by Tenant to Landlord of (a) a statement (a " Fund Request ") setting forth the total amount of the TI Allowance requested, (b) a summary of the Tenant Improvements performed using AIA standard form Application for Payment (G 702) executed by the general contractor and by the architect, (c) invoices from the general contractor, the architect, and any subcontractors, material suppliers and other parties requesting payment with respect to the amount of the TI Allowance then being requested, (d) unconditional lien

releases from the general contractor and each subcontractor and material supplier with respect to previous payments made by either Landlord or Tenant for the Tenant Improvements in a form acceptable to Landlord and complying with Applicable Laws and (e) conditional lien releases from the general contractor and each subcontractor and material supplier with respect to the Tenant Improvements performed that correspond to the Fund Request each in a form acceptable to Landlord and complying with Applicable Laws, then Landlord shall, within thirty (30) days following receipt by Landlord of a Fund Request and the accompanying materials required by this Section, pay to (as elected by Landlord) the applicable contractors, subcontractors and material suppliers or Tenant (for reimbursement for payments made by Tenant to such contractors, subcontractors or material suppliers either prior to Landlord's approval of the Approved TI Budget or as a result of Tenant's decision to pay for the Tenant Improvements itself and later seek reimbursement from Landlord in the form of one lump sum payment in accordance with the Lease and this Work Letter), the amount of Tenant Improvement costs set forth in such Fund Request; provided, however, that Landlord shall not be obligated to make any payments under this Section until the budget for the Tenant Improvements is approved in accordance with Section 6.2, and any Fund Request under this Section shall be subject to the payment limits set forth in Section 6.2 above and Article 4 of the Lease. Notwithstanding anything in this Section to the contrary, Tenant shall not submit a Fund Request more often than every thirty (30) days. Any additional Fund Requests submitted by Tenant shall be void and of no force or effect.

6.4. Accrual Information. In addition to the other requirements of this Section 6, Tenant shall, no later than the second (2nd) business day of each month until the Tenant Improvements are complete, provide Landlord with an estimate of (a) the percentage of design and other soft cost work that has been completed, (b) design and other soft costs spent through the end of the previous month, both from commencement of the Tenant Improvements and solely for the previous month, (c) the percentage of construction and other hard cost work that has been completed, (d) construction and other hard costs spent through the end of the previous month, both from commencement of the Tenant Improvements and solely for the previous month, and (e) the estimated date of Substantial Completion of the Tenant Improvements.

7. Miscellaneous.

7.1. Incorporation of Lease Provisions. Sections 40.6 through 40.19 of the Lease are incorporated into this Work Letter by reference, and shall apply to this Work Letter in the same way that they apply to the Lease.

7.2. General. Except as otherwise set forth in the Lease or this Work Letter, this Work Letter shall not apply to improvements performed in any additional premises added to the Premises at any time or from time to time, whether by any options under the Lease or otherwise; or to any portion of the Premises or any additions to the Premises in the event of a renewal or extension of the original Term, whether by any options under the Lease or otherwise, unless the Lease or any amendment or supplement to the Lease expressly provides that such additional premises are to be delivered to Tenant in the same condition as the initial Premises.

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IN WITNESS WHEREOF, Landlord and Tenant have executed this Work Letter to be effective on the date first above written.

LANDLORD :

BMR-PACIFIC RESEARCH CENTER LP,
a Delaware limited partnership

By: _____
Name: _____
Title: _____

TENANT :

PROTAGONIST THERAPEUTICS, INC.,
a Delaware corporation

By: _____
Name: _____
Title: _____

EXHIBIT B-1

TENANT WORK INSURANCE SCHEDULE

Tenant shall be responsible for requiring all of Tenant contractors doing construction or renovation work to purchase and maintain such insurance as shall protect it from the claims set forth below which may arise out of or result from any Tenant Work whether such Tenant Work is completed by Tenant or by any Tenant contractors or by any person directly or indirectly employed by Tenant or any Tenant contractors, or by any person for whose acts Tenant or any Tenant contractors may be liable:

1. Claims under workers' compensation, disability benefit and other similar employee benefit acts which are applicable to the Tenant Work to be performed.

2. Claims for damages because of bodily injury, occupational sickness or disease, or death of employees under any applicable employer's liability law.

3. Claims for damages because of bodily injury, or death of any person other than Tenant's or any Tenant contractors' employees.

4. Claims for damages insured by usual personal injury liability coverage which are sustained (a) by any person as a result of an offense directly or indirectly related to the employment of such person by Tenant or any Tenant contractors or (b) by any other person.

5. Claims for damages, other than to the Tenant Work itself, because of injury to or destruction of tangible property, including loss of use therefrom.

6. Claims for damages because of bodily injury or death of any person or property damage arising out of the ownership, maintenance or use of any motor vehicle.

Tenant contractors' Commercial General Liability Insurance shall include premises/operations (including explosion, collapse and underground coverage if such Tenant Work involves any underground work), elevators, independent contractors, products and completed operations, and blanket contractual liability on all written contracts, all including broad form property damage coverage.

Tenant contractors' Commercial General, Automobile, Employers and Umbrella Liability Insurance shall be written for not less than limits of liability as follows:

a. Commercial General Liability:	
Bodily Injury and Property Damage	Commercially reasonable amounts, but in any event no less than $1,000,000 per occurrence and $2,000,000 general aggregate, with $2,000,000 products and completed operations aggregate.

b. Commercial Automobile Liability:	$1,000,000 per accident
Bodily Injury and Property Damage	
c. Employer's Liability:	
Each Accident	$500,000
Disease – Policy Limit	$500,000
Disease – Each Employee	$500,000
d. Umbrella Liability:	Commercially reasonable amounts (excess of coverages a, b and c above), but in any event no less than $5,000,000 per occurrence / aggregate.
Bodily Injury and Property Damage	

All subcontractors for Tenant contractors shall carry the same coverages and limits as specified above, unless different limits are reasonably approved by Landlord. The foregoing policies shall contain a provision that coverages afforded under the policies shall not be canceled or not renewed until at least thirty (30) days' prior written notice has been given to the Landlord. Certificates of insurance including required endorsements showing such coverages to be in force shall be filed with Landlord prior to the commencement of any Tenant Work and prior to each renewal. Coverage for completed operations must be maintained for the lesser of ten (10) years and the applicable statue of repose following completion of the Tenant Work, and certificates evidencing this coverage must be provided to Landlord. The minimum A.M. Best's rating of each insurer shall be A- VII. Landlord and its mortgagees shall be named as additional insureds under Tenant contractors' Commercial General Liability, Commercial Automobile Liability and Umbrella Liability Insurance policies as respects liability arising from work or operations performed, or ownership, maintenance or use of autos, by or on behalf of such contractors. Each contractor and its insurers shall provide waivers of subrogation with respect to any claims covered or that should have been covered by valid and collectible insurance, including any deductibles or self-insurance maintained thereunder.

If any contractor's work involves the handling or removal of asbestos (as determined by Landlord in its sole and absolute discretion), such contractor shall also carry Pollution Legal Liability insurance. Such coverage shall include bodily injury, sickness, disease, death or mental anguish or shock sustained by any person; property damage, including physical injury to or destruction of tangible property (including the resulting loss of use thereof), clean-up costs and the loss of use of tangible property that has not been physically injured or destroyed; and defense costs, charges and expenses incurred in the investigation, adjustment or defense of claims for such damages. Coverage shall apply to both sudden and non-sudden pollution conditions including the discharge, dispersal, release or escape of smoke, vapors, soot, fumes, acids, alkalis, toxic chemicals, liquids or gases, waste materials or other irritants, contaminants or pollutants into or upon land, the atmosphere or any watercourse or body of water. Claims-made coverage is permitted, provided the policy retroactive date is continuously maintained prior to the Term Commencement Date, and coverage is continuously maintained during all periods in which Tenant occupies the Premises. Coverage shall be maintained with limits of not less than $1,000,000 per incident with a $2,000,000 policy aggregate.

EXHIBIT C

ACKNOWLEDGEMENT OF TERM COMMENCEMENT DATE
AND TERM EXPIRATION DATE

THIS ACKNOWLEDGEMENT OF TERM COMMENCEMENT DATE AND TERM EXPIRATION DATE is entered into as of [ ], 2017, with reference to that certain Lease (the " Lease ") dated as of [ ], 2017, by PROTAGONIST THERAPEUTICS, INC., a Delaware corporation (" Tenant "), in favor of BMR-PACIFIC RESEARCH CENTER LP, a Delaware limited partnership (" Landlord "). All capitalized terms used herein without definition shall have the meanings ascribed to them in the Lease.

Tenant hereby confirms the following:

1. Tenant accepted possession of the Premises for construction of improvements or the installation of personal or other property on [ ], 20[ ], and for use in accordance with the Permitted Use on [ ], 20[ ]. Tenant first occupied the Premises for the Permitted Use on [ ], 20[ ].

2. The Premises are in good order, condition and repair.

3. The Tenant Improvements are Substantially Complete.

4. All conditions of the Lease to be performed by Landlord as a condition to the full effectiveness of the Lease have been satisfied, and Landlord has fulfilled all of its duties in the nature of inducements offered to Tenant to lease the Premises.

5. In accordance with the provisions of Article 4 of the Lease, the Term Commencement Date is [ ], 20[ ], and, unless the Lease is terminated prior to the Term Expiration Date pursuant to its terms, the Term Expiration Date shall be [ ], 20[ ].

6. The Lease is in full force and effect, and the same represents the entire agreement between Landlord and Tenant concerning the Premises[, except [ ]].

7. Tenant has no existing defenses against the enforcement of the Lease by Landlord, and there exist no offsets or credits against Rent owed or to be owed by Tenant.

8. The obligation to pay Rent is presently in effect and all Rent obligations on the part of Tenant under the Lease commenced to accrue on [ ], 20[ ], with Base Rent payable on the dates and amounts set forth in the chart below:

Dates	Approximate Square Feet of Rentable Area	Base Rent per Square Foot of Rentable Area	Monthly Base Rent
[ ]/[ ]/[ ]-[ ]/[ ]/[ ]	[ ]	$[ ] monthly	[ ]

9. The undersigned Tenant has not made any prior assignment, transfer, hypothecation or pledge of the Lease or of the rents thereunder or sublease of the Premises or any portion thereof.

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IN WITNESS WHEREOF, Tenant has executed this Acknowledgment of Term Commencement Date and Term Expiration Date as of the date first written above.

TENANT:

PROTAGONIST THERAPEUTICS, INC.,
a Delaware corporation

By: _____
Name: _____
Title: _____

EXHIBIT D

FF&E

2 Televisions

1 Multimedia projector and screen

1 formal boardroom table and 12 leather chairs

1 small conference room table and 8 leather chairs

1 small conference room table and 6 leather chairs

1 reception desk

Approx. 18 cubicle stations

Approx. 18 office tables + chairs on the 2 nd floor

Approx. 15 office tables + chairs on the 1 st floor

Approx. 30 break room chairs (orange)

Approx. 6 rest/lounge area chairs

EXHIBIT E

FORM OF LETTER OF CREDIT

[On letterhead or L/C letterhead of Issuer]

LETTER OF CREDIT

Date: _____, 20 __

_____(the " Beneficiary ")
_____
_____
Attention: _____
L/C. No.: _____
Loan No.: _____

Ladies and Gentlemen:

We establish in favor of Beneficiary our irrevocable and unconditional Letter of Credit numbered as identified above (the " L/C ") for an aggregate amount of $ _____, expiring at _____:00 p.m. on _____or, if such day is not a Banking Day, then the next succeeding Banking Day (such date, as extended from time to time, the " Expiry Date "). " Banking Day " means a weekday except a weekday when commercial banks in _____are authorized or required to close.

We authorize Beneficiary to draw on us (the " Issuer ") for the account of _____(the " Account Party "), under the terms and conditions of this L/C.

Funds under this L/C are available by presenting the following documentation (the " Drawing Documentation "): (a) the original L/C and (b) a sight draft substantially in the form of Attachment 1 , with blanks filled in and bracketed items provided as appropriate. No other evidence of authority, certificate, or documentation is required.

Drawing Documentation must be presented at Issuer's office at _____on or before the Expiry Date by personal presentation, courier or messenger service, or fax. Presentation by fax shall be effective upon electronic confirmation of transmission as evidenced by a printed report from the sender's fax machine. After any fax presentation, but not as a condition to its effectiveness, Beneficiary shall with reasonable promptness deliver the original Drawing Documentation by any other means. Issuer will on request issue a receipt for Drawing Documentation.

We agree, irrevocably, and irrespective of any claim by any other person, to honor drafts drawn under and in conformity with this L/C, within the maximum amount of this L/C, presented to us on or before the Expiry Date, provided we also receive (on or before the Expiry Date) any other Drawing Documentation this L/C requires.

We shall pay this L/C only from our own funds by check or wire transfer, in compliance with the Drawing Documentation.

If Beneficiary presents proper Drawing Documentation to us on or before the Expiry Date, then we shall pay under this L/C at or before the following time (the " Payment Deadline "): (a) if presentment is made at or before noon of any Banking Day, then the close of such Banking Day; and (b) otherwise, the close of the next Banking Day. We waive any right to delay payment beyond the Payment Deadline. If we determine that Drawing Documentation is not proper, then we shall so advise Beneficiary in writing, specifying all grounds for our determination, within one Banking Day after the Payment Deadline.

Partial drawings are permitted. This L/C shall, except to the extent reduced thereby, survive any partial drawings.

We shall have no duty or right to inquire into the validity of or basis for any draw under this L/C or any Drawing Documentation. We waive any defense based on fraud or any claim of fraud.

The Expiry Date shall automatically be extended by one year (but never beyond (the " Outside Date ")) unless, on or before the date 90 days before any Expiry Date, we have given Beneficiary notice that the Expiry Date shall not be so extended (a " Nonrenewal Notice "). We shall promptly upon request confirm any extension of the Expiry Date under the preceding sentence by issuing an amendment to this L/C, but such an amendment is not required for the extension to be effective. We need not give any notice of the Outside Date.

Beneficiary may from time to time without charge transfer this L/C, in whole but not in part, to any transferee (the " Transferee "). Issuer shall look solely to Account Party for payment of any fee for any transfer of this L/C. Such payment is not a condition to any such transfer. Beneficiary or Transferee shall consummate such transfer by delivering to Issuer the original of this L/C and a Transfer Notice substantially in the form of Attachment 2 , purportedly signed by Beneficiary, and designating Transferee. Issuer shall promptly reissue or amend this L/C in favor of Transferee as Beneficiary. Upon any transfer, all references to Beneficiary shall automatically refer to Transferee, who may then exercise all rights of Beneficiary. Issuer expressly consents to any transfers made from time to time in compliance with this paragraph.

Any notice to Beneficiary shall be in writing and delivered by hand with receipt acknowledged or by overnight delivery service such as FedEx (with proof of delivery) at the above address, or such other address as Beneficiary may specify by written notice to Issuer. A copy of any such notice shall also be delivered, as a condition to the effectiveness of such notice, to: (or such replacement as Beneficiary designates from time to time by written notice).

No amendment that adversely affects Beneficiary shall be effective without Beneficiary's written consent.

This L/C is subject to and incorporates by reference: (a) the International Standby Practices 98 (" ISP 98 "); and (b) to the extent not inconsistent with ISP 98, Article 5 of the Uniform Commercial Code of the State of New York.

Very truly yours,

[Issuer Signature]

ATTACHMENT 1 TO EXHIBIT E

FORM OF SIGHT DRAFT

[BENEFICIARY LETTERHEAD]

TO:

[Name and Address of Issuer]

SIGHT DRAFT

AT SIGHT, pay to the Order of _____, the sum of _____United States Dollars ($ ____). Drawn under [Issuer] Letter of Credit No. _____ dated _____.

[Issuer is hereby directed to pay the proceeds of this Sight Draft solely to the following account: _____.]

[Name and signature block, with signature or purported signature of Beneficiary]

Date: _____

ATTACHMENT 2 TO EXHIBIT E

FORM OF TRANSFER NOTICE

[BENEFICIARY LETTERHEAD]

TO:

[Name and Address of Issuer] (the "Issuer")

TRANSFER NOTICE

By signing below, the undersigned, Beneficiary (the "Beneficiary") under Issuer's Letter of Credit No. _____ dated _____ (the "L/C"), transfers the L/C to the following transferee (the "Transferee"):

[Transferee Name and Address]

The original L/C is enclosed. Beneficiary directs Issuer to reissue or amend the L/C in favor of Transferee as Beneficiary. Beneficiary represents and warrants that Beneficiary has not transferred, assigned, or encumbered the L/C or any interest in the L/C, which transfer, assignment, or encumbrance remains in effect.

[Name and signature block, with signature or purported signature of Beneficiary]

Date: _____

EXHIBIT F

RULES AND REGULATIONS

NOTHING IN THESE RULES AND REGULATIONS (" RULES AND REGULATIONS ") SHALL SUPPLANT ANY PROVISION OF THE LEASE. IN THE EVENT OF A CONFLICT OR INCONSISTENCY BETWEEN THESE RULES AND REGULATIONS AND THE LEASE, THE LEASE SHALL PREVAIL.

1. No Tenant Party shall encumber or obstruct the common entrances, lobbies, elevators, sidewalks and stairways of the Building(s) or the Project or use them for any purposes other than ingress or egress to and from the Building(s) or the Project.

2. Except as specifically provided in the Lease, no sign, placard, picture, advertisement, name or notice shall be installed or displayed on any part of the outside of the Premises or the Building(s) without Landlord's prior written consent. Landlord shall have the right to remove, at Tenant's sole cost and expense and without notice, any sign installed or displayed in violation of this rule.

3. If Landlord objects in writing to any curtains, blinds, shades, screens, hanging plants or other similar objects attached to or used in connection with any window or door of the Premises or placed on any windowsill, and (a) such window, door or windowsill is visible from the exterior of the Premises and (b) such curtain, blind, shade, screen, hanging plant or other object is not included in plans approved by Landlord, then Tenant shall promptly remove such curtains, blinds, shades, screens, hanging plants or other similar objects at its sole cost and expense.

4. No deliveries shall be made that impede or interfere with other tenants in or the operation of the Project. Movement of furniture, office equipment or any other large or bulky material(s) through the Common Area shall be restricted to such hours as Landlord may designate and shall be subject to reasonable restrictions that Landlord may impose.

5. Tenant shall not place a load upon any floor of the Premises that exceeds the load per square foot that (a) such floor was designed to carry or (b) is allowed by Applicable Laws. Fixtures and equipment that cause noises or vibrations that may be transmitted to the structure of the Building(s) to such a degree as to be objectionable to other tenants shall be placed and maintained by Tenant, at Tenant's sole cost and expense, on vibration eliminators or other devices sufficient to eliminate such noises and vibrations to levels reasonably acceptable to Landlord and the affected tenants of the Project.

6. Tenant shall not use any method of HVAC other than that approved in writing by Landlord or present at the Project and serving the Premises as of the Execution Date.

7. Tenant shall not install any radio, television or other antennae; cell or other communications equipment; or other devices on the roof or exterior walls of the Premises except in accordance with the Lease. Tenant shall not interfere with radio, television or other digital or electronic communications at the Project or elsewhere.

8. Canvassing, peddling, soliciting and distributing handbills or any other written material within, on or around the Project (other than within the Premises) are prohibited. Tenant shall cooperate with Landlord to prevent such activities by any Tenant Party.

9. Tenant shall store all of its trash, garbage and Hazardous Materials in receptacles within its Premises or in receptacles designated by Landlord outside of the Premises. Tenant shall not place in any such receptacle any material that cannot be disposed of in the ordinary and customary manner of trash, garbage and Hazardous Materials disposal. Any Hazardous Materials transported through Common Area shall be held in secondary containment devices. Tenant shall be responsible, at its sole cost and expense, for Tenant's removal of its trash, garbage and Hazardous Materials. Tenant is encouraged to participate in the waste removal and recycling program in place at the Project.

10. The Premises shall not be used for lodging or for any improper, immoral or objectionable purpose. No cooking shall be done or permitted in the Premises; provided , however, that Tenant may use (a) equipment approved in accordance with the requirements of insurance policies that Landlord or Tenant is required to purchase and maintain pursuant to the Lease for brewing coffee, tea, hot chocolate and similar beverages, (b) microwave ovens for employees' use and (c) equipment shown on Tenant Improvement plans approved by Landlord; provided , further, that any such equipment and microwave ovens are used in accordance with Applicable Laws.

11. Tenant shall not, without Landlord's prior written consent, use the name of the Project, if any, in connection with or in promoting or advertising Tenant's business except as Tenant's address.

12. Tenant shall comply with all safety, fire protection and evacuation procedures and regulations established by Landlord or any Governmental Authority.

13. Tenant assumes any and all responsibility for protecting the Premises from theft, robbery and pilferage, which responsibility includes keeping doors locked and other means of entry to the Premises closed.

14. Tenant shall not modify any locks to the Premises without Landlord's prior written consent, which consent Landlord shall not unreasonably withhold, condition or delay. Tenant shall furnish Landlord with copies of keys, pass cards or similar devices for locks to the Premises.

15. Tenant shall cooperate and participate in all reasonable security programs affecting the Premises.

16. Tenant shall not permit any animals in the Project, other than for service animals or for use in laboratory experiments.

17. Bicycles shall not be taken into the Building(s) (including the elevators and stairways of the Building) except into areas designated by Landlord.

18. The water and wash closets and other plumbing fixtures shall not be used for any purposes other than those for which they were constructed, and no sweepings, rubbish, rags or other substances shall be deposited therein.

19. Discharge of industrial sewage shall only be permitted if Tenant, at its sole expense, first obtains all necessary permits and licenses therefor from all applicable Governmental Authorities.

20. Smoking is prohibited inside the Buildings, except in designated outdoor areas of the Project (if any).

21. The Project's hours of operation are currently 24 hours a day seven days a week.

22. Tenant shall comply with all orders, requirements and conditions now or hereafter imposed by Applicable Laws or Landlord (" Waste Regulations ") regarding the collection, sorting, separation and recycling of waste products, garbage, refuse and trash generated by Tenant (collectively, " Waste Products "), including (without limitation) the separation of Waste Products into receptacles reasonably approved by Landlord and the removal of such receptacles in accordance with any collection schedules prescribed by Waste Regulations.

23. Tenant, at Tenant's sole cost and expense, shall cause the Premises to be exterminated on a monthly basis to Landlord's reasonable satisfaction and shall cause all portions of the Premises used for the storage, preparation, service or consumption of food or beverages to be cleaned daily in a manner reasonably satisfactory to Landlord, and to be treated against infestation by insects, rodents and other vermin and pests whenever there is evidence of any infestation. Tenant shall not permit any person to enter the Premises or the Project for the purpose of providing such extermination services, unless such persons have been approved by Landlord. If requested by Landlord, Tenant shall, at Tenant's sole cost and expense, store any refuse generated in the Premises by the consumption of food or beverages in a cold box or similar facility.

24. If Tenant desires to use any portion of the Common Area for a Tenant-related event, Tenant must notify Landlord in writing at least thirty (30) days prior to such event on the form attached as Attachment 1 to this Exhibit, which use shall be subject to Landlord's prior written consent, not to be unreasonably withheld, conditioned or delayed. Notwithstanding anything in this Lease or the completed and executed Attachment to the contrary, Tenant shall be solely responsible for setting up and taking down any equipment or other materials required for the event, and shall promptly pick up any litter and report any property damage to Landlord related to the event. Any use of the Common Area pursuant to this Section shall be subject to the provisions of Article 28 of the Lease.

Landlord may waive any one or more of these Rules and Regulations for the benefit of Tenant or any other tenant, but no such waiver by Landlord shall be construed as a waiver of such Rules and Regulations in favor of Tenant or any other tenant, nor prevent Landlord from thereafter enforcing any such Rules and Regulations against any or all of the tenants of the Project, including Tenant. These Rules and Regulations are in addition to, and shall not be construed to in any way modify or amend, in whole or in part, the terms covenants, agreements and conditions of the Lease. Landlord reserves the right to make such other and reasonable

additional rules and regulations as, in its judgment, may from time to time be needed for safety and security, the care and cleanliness of the Project, or the preservation of good order therein; provided , however, that Tenant shall not be obligated to adhere to such additional rules or regulations until Landlord has provided Tenant with written notice thereof. Tenant agrees to abide by these Rules and Regulations and any such additional rules and regulations issued or adopted by Landlord. Tenant shall be responsible for the observance of these Rules and Regulations by all Tenant Parties.

ATTACHMENT 1 TO EXHIBIT F

REQUEST FOR USE OF COMMON AREA

REQUEST FOR USE OF COMMON AREA

Date of Request: _____

Landlord/Owner: _____

Tenant/Requestor: _____

Property Location: _____

Event Description: _____

_____

_____

Proposed Plan for Security & Cleaning: _____

_____

_____

Date of Event: _____

Hours of Event: (to include set-up and take down): _____

Location at Property (see attached map): _____

Number of Attendees: _____

Open to the Public? ☐ YES ☐ NO

Food and/or Beverages? ☐ YES ☐ NO

If YES:

- Will food be prepared on site? ☐ YES ☐ NO
- Please describe: _____
- Will alcohol be served? ☐ YES ☐ NO
- Please describe: _____
- Will attendees be charged for alcohol? ☐ YES ☐ NO

- Is alcohol license or permit required? ☐ YES ☐ NO
- Does caterer have alcohol license or permit: ☐ YES ☐ NO ☐ N/A

Other Amenities (tent, booths, band, food trucks, bounce house, etc.): _____

_____

_____

Other Event Details or Special Circumstances: _____

_____

_____

_____

_____

The undersigned certifies that the foregoing is true, accurate and complete and he/she is duly authorized to sign and submit this request on behalf of the Tenant/Requestor named above.

PROTAGONIST THERAPEUTICS, INC.,
a Delaware corporation

By: _____
Name: _____
Title: _____
Date: _____

EXHIBIT G

APPROVED VENDOR LIST

None.

EXHIBIT H

TENANT'S PROPERTY

None.

EXHIBIT I

FORM OF ESTOPPEL CERTIFICATE

To: BMR-Pacific Research Center LP
17190 Bernardo Center Drive
San Diego, California 92128
Attention: Legal Department

BioMed Realty, L.P.
17190 Bernardo Center Drive
San Diego, California 92128

Re: First and second floors (the " Premises ") at 7707 Gateway Boulevard, Newark, California (the " Property ")

The undersigned tenant (" Tenant ") hereby certifies to you as follows:

1. Tenant is a tenant at the Property under a lease (the " Lease ") for the Premises dated as of [_____], 20[___]. The Lease has not been cancelled, modified, assigned, extended or amended [except as follows: [_____]], and there are no other agreements, written or oral, affecting or relating to Tenant's lease of the Premises or any other space at the Property. The lease term expires on [_____], 20[___].

2. Tenant took possession of the Premises, currently consisting of [_____] square feet, on [_____], 20[___], and commenced to pay rent on [_____], 20[___]. Tenant has full possession of the Premises, has not assigned the Lease or sublet any part of the Premises, and does not hold the Premises under an assignment or sublease[, except as follows: [_____]].

3. All base rent, rent escalations and additional rent under the Lease have been paid through [_____], 20[___]. There is no prepaid rent[, except $[_____]][, and the amount of security deposit is $[_____] [in cash][OR][in the form of a letter of credit]]. Tenant currently has no right to any future rent abatement under the Lease.

4. Base rent is currently payable in the amount of $[_____] per month.

5. Tenant is currently paying estimated payments of additional rent of $[_____] per month on account of real estate taxes, insurance, management fees and Common Area maintenance expenses.

6. All work to be performed for Tenant under the Lease has been performed as required under the Lease and has been accepted by Tenant[, except [_____]], and all allowances to be paid to Tenant, including allowances for tenant improvements, moving expenses or other items, have been paid.

7. The Lease is in full force and effect, free from default to Tenant's knowledge and free from any event that could become a default under the Lease to Tenant's knowledge, and to Tenant's knowledge, Tenant has no claims against the landlord or offsets or defenses against rent, and there are no disputes with the landlord. Tenant has received no notice of prior sale, transfer, assignment, hypothecation or pledge of the Lease or of the rents payable thereunder[, except [_____]].

8. Tenant has no rights or options to purchase the Property.

9. To Tenant's knowledge, no hazardous wastes have been generated, treated, stored or disposed of by or on behalf of Tenant in, on or around the Premises or the Project in violation of any environmental laws.

10. The undersigned has executed this Estoppel Certificate with the knowledge and understanding that [INSERT NAME OF LANDLORD, PURCHASER OR LENDER, AS APPROPRIATE] or its assignee is [acquiring the Property/making a loan secured by the Property] in reliance on this certificate and that the undersigned shall be bound by this certificate. The statements contained herein may be relied upon by [INSERT NAME OF PURCHASER OR LENDER, AS APPROPRIATE], BMR-Pacific Research Center LP, BioMed Realty, L.P., BRE-Edison Parent L.P., and any [other] mortgagee of the Property and their respective successors and assigns.

Any capitalized terms not defined herein shall have the respective meanings given in the Lease.

Dated this [ ] day of [ ], 20[ ].

PROTAGONIST THERAPEUTICS, INC.,
a Delaware corporation

By: _____
Name: _____
Title: _____

EXHIBIT J

LANDLORD WORK AREA

Exhibit 21.1

SUBSIDIARIES OF PROTAGONIST THERAPEUTICS, INC.

Subsidiary	Jurisdiction of Formation/Organization
Protagonist Pty Limited	Australia

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in the Registration Statement on Form S-8 (No. 333-213120) of Protagonist Therapeutics, Inc. of our report dated March 7, 2017 relating to the consolidated financial statements, which appears in this Form 10-K.

/s/ PricewaterhouseCoopers LLP

San Jose, CA
March 7, 2017

Exhibit 31.1

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

I, Dinesh V. Patel, certify that:

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

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

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

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

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

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

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

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

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

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

/s/ Dinesh V. Patel, Ph.D.

Date: March 7, 2017

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

Exhibit 31.2

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

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

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

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

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

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

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

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

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

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

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

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

/s/ Thomas P. O'Neil

Date: March 7, 2017

Thomas P. O'Neil
Chief Financial Officer

Exhibit 32.1

CERTIFICATION OF CHIEF EXECUTIVE OFFICER AND CHIEF FINANCIAL OFFICER

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

1. The Company's Annual Report on Form 10-K for the period ended December 31, 2016 (the "Annual Report"), to which this Certification is attached as Exhibit 32.1, fully complies with the requirements of Section 13(a) or Section 15(d) of the Exchange Act; and

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

/s/ Dinesh V. Patel, Ph.D.

Date: March 7, 2017

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

/s/ Thomas P. O'Neil

Date: March 7, 2017

Thomas P. O'Neil
Chief Financial Officer

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