UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

Form 10-K

(Mark One)

☒ **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 number: 001-37378

ATYR PHARMA, INC.

(Exact Name of Registrant as Specified in its Charter)

Delaware	**20-3435077**
(State or Other Jurisdiction of Incorporation or Organization)	**(I.R.S. Employer Identification No.)**
3545 John Hopkins Court, Suite #250, San Diego, CA	**92121**
(Address of Principal Executive Offices)	**(Zip Code)**

(858) 731-8389
(Registrant's Telephone Number, Including Area Code)

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

Title of Each Class	**Name of Each Exchange on Which Registered**
Common Stock, par value $0.001 per share	**The NASDAQ Global Select 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 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 S-K is not contained herein, and will not be contained, to the best of the registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☒

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 definitions of "large accelerated filer", "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer ☐ Accelerated filer ☐ Non-accelerated filer ☐ Smaller reporting company ☒

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

The aggregate market value of the registrant's common stock held by non-affiliates of the registrant was approximately $37,197,028 based on the closing price of the registrant's common stock on the Nasdaq Global Select Market of $2.78 per share on June 30, 2016. Shares of common stock held by each executive officer and director and each person who beneficially owns 10% or more of the outstanding common stock have been excluded from this calculation. This determination of affiliate status may not be conclusive for other purposes.

The number of outstanding shares of the registrant's common stock, par value $0.001 per share, as of March 8, 2017 was 23,748,096.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's proxy statement to be filed with the Securities and Exchange Commission, or SEC, pursuant to Regulation 14A in connection with the registrant's 2017 Annual Meeting of Stockholders, which will be filed subsequent to the date hereof, are incorporated by reference into Part III of this annual report on Form 10-K. Such proxy statement will be filed with the SEC not later than 120 days following the end of the registrant's fiscal year ended December 31, 2016.

ATYR PHARMA, INC.

ANNUAL REPORT ON FORM 10-K

For the Fiscal Year Ended December 31, 2016

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In this Annual Report on Form 10-K, Annual Report, unless the context requires otherwise, "aTyr Pharma," "aTyr," "Company," "we," "our," and "us" means aTyr Pharma, Inc. and its subsidiary, Pangu BioPharma Limited.

The market data and certain other statistical information used in this Annual Report are based on independent industry publications, governmental publications, reports by market research firms or other independent sources. Some data are also based on our good faith estimates. Information that is based on estimates, forecasts, projections, market research or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information.

We own various U.S. federal trademark applications and unregistered trademarks, including our company name, Resolaris™ and Stalaris™. All other trademarks or trade names referred to in this Annual Report are the property of their respective owners. Solely for convenience, the trademarks and trade names in this prospectus are referred to without the symbols ® and ™, but such references should not be construed as any indicator that their respective owners will not assert, to the fullest extent under applicable law, their rights thereto.

Forward-Looking Statements

This Annual Report on Form 10-K contains “forward-looking statements” that involve risks and uncertainties, as well as assumptions that even if they never materialize or prove incorrect, could cause our results to differ materially from those expressed or implied by such forward-looking statements. We make such forward-looking statements pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995 and other federal securities laws. All statements other than statements of historical facts contained in this Annual Report on Form 10-K are forward-looking statements. In some cases, you can identify forward-looking statements by terms such as "may," "will," "expect," "anticipate," "estimate," "intend," "plan," "predict," "potential," "believe," "should" and similar expressions. Forward-looking statements in this Annual Report on Form 10-K include, but are not limited to, statements about:

- the success, cost and timing of our clinical trials, including our ongoing Phase 1b/2 trials of Resolaris and planned clinical trials for Stalaris, and whether the results of our trials will be sufficient to support domestic or foreign regulatory approvals;
- the likelihood and timing of regulatory approvals for Resolaris, Stalaris and any of our other product candidates;
- our ability to identify and discover additional product candidates;
- whether our existing capital resources will be sufficient to enable us to complete any particular portion of our planned clinical development of Resolaris, Stalaris and other product candidates;
- our ability to obtain, maintain, defend and enforce intellectual property rights protecting our product candidates;
- our estimates of our expenses, ongoing losses, future revenue, capital requirements and our needs for or ability to obtain additional financing;
- performance of third-party service providers and independent contractors upon whom we rely to conduct our clinical trials and to manufacture our product candidates or certain components of our product candidates;
- our ability to develop sales and marketing capabilities or to enter into strategic partnerships to develop and commercialize Resolaris, Stalaris or any of our other product candidates;
- the timing and success of the commercialization of Resolaris, Stalaris or any of our other product candidates;
- the rate and degree of market acceptance of our product candidates;
- the size and growth of the potential markets for our product candidates and our ability to serve those markets;
- regulatory developments in the United States and foreign countries;
- the success of competing therapies that are or may become available;
- our ability to attract and retain key scientific, medical or management personnel; and
- other risks and uncertainties, including those described under Part I, Item 1A, Risk Factors in this Annual Report on Form 10-K.

The cautionary statements made in this report are intended to be applicable to all related forward-looking statements wherever they may appear in this report. We urge you not to place undue reliance on these forward-looking statements, which speak only as of the date of this report. Except as required by law, we assume no obligation to update our forward-looking statements, even if new information becomes available in the future.

PART I

Item 1. Business

Overview

We engage in the discovery and clinical development of innovative medicines for patients suffering from severe, rare diseases using our knowledge of Physiocrine biology, a newly discovered set of physiological pathways. Through our research efforts, we believe that Physiocrines evolved over billions of years to promote homeostasis in complex organisms. We have evidence to support that some of these proteins evolved to govern and orchestrate the mammalian immune system. We believe immune imbalance is underappreciated in many disease types and may ultimately be responsible for much of the pathophysiology associated with a number of important genetic and immunology based diseases.

By focusing on immune pathways in disease, we believe our therapeutic candidates have the potential to restore patients to a healthier state, achieve homeostatic balance and ultimately lead to improved clinical outcomes. To date, our discovery efforts have generated three immunology-based investigational innovative therapeutic programs in three different therapeutic areas:

- **Resolaris**: We internally discovered and developed Resolaris, our first Physiocrine-based therapeutic candidate, based on a protein naturally secreted from muscle that acts on T-cells at the tissue level to promote healthier muscle. We believe this may translate into an innovative therapeutic for rare genetic myopathies with an immune component (e.g. T-cells in the patients' muscle), including limb-girdle muscular dystrophy (LGMD), facioscapulohumeral muscular dystrophy (FSHD), and Duchenne muscular dystrophy (DMD). Resolaris also represents an example of our first therapeutic modality - natural protein therapy – adding back a pathway that is insufficiently produced by the human body to counteract disease.
- **Stalaris:** Our scientists successfully engineered the first fusion protein with a Physiocrine, Stalaris, to provide designed properties to enhance the immuno-modulatory aspects of a Physiocrine *in vivo*. We plan to develop Stalaris as a potential therapeutic for patients with rare pulmonary diseases with an immune component, including interstitial lung disease. This fusion protein, which utilizes the Fc region of an antibody, also potentially represents a novel Fc-Physiocrine platform for future Physiocrine-based therapies.
- **Project ORCA:** Our third program, represents a third therapeutic modality distinct from Resolaris or Stalaris. It also diversifies our pipeline by addressing severe diseases in a therapeutic area that differs from those of our first two programs. We use code name "Project ORCA" for this preclinical research program.

We believe therapies that can harness the power of the immune system represent an important frontier of transformational medicines. All of our current programs focus on modulating the immune system in an effort to create better clinical outcomes for patients. Our preclinical work increases our confidence that certain Physiocrines can be used to modulate immune cell activity, especially activated T-cells. Based on our clinical results to date, we believe Resolaris has a favorable safety and tolerability profile with no observed signs of general immunosuppression, which could give Resolaris a competitive advantage over current immunosuppressive agents (e.g. steroids). We have also observed promising signals of clinical activity in patients treated with Resolaris in our clinical studies, including improved muscle strength in certain patients, which we find encouraging to our therapeutic hypothesis.

Discoveries of new physiological pathways have been responsible for profound advancements in the field of medicine resulting in better patient outcomes and disruptive advantages for the industry's therapeutic development pipeline. Such discoveries include homeostatic pathways, which gave rise to agonists such as insulin and erythropoietin, as well as antagonists to the tumor necrosis factor (TNF), the vascular endothelial growth factor (VEGF), and the complement pathways.

Our expansive Physiocrine patent estate provides us with potential product protection as we pioneer this new and important area of human biology. To protect our industry unique pipeline based on our proprietary new biology, we have built an intellectual property estate comprising over 175 issued patents or allowed patent applications that are owned or exclusively licensed by us, including over 300 potential Physiocrine-based protein compositions. We believe it is in the best interest of our stakeholders, including patients, caregivers, and our stockholders, to advance one or more of our three current programs based on Physiocrine biology with the expertise of or funding from appropriate strategic partners.

Strategy

We aim to capitalize on Physiocrine biology to develop novel, first-in-class medicines with industry unique mechanisms to treat patients with severe, rare diseases where immunology is important to the disease process. Key elements of our strategy include the following:

- ***Leverage our leadership position in new pathways in immunology based on Physiocrine biology.*** As we continue to research and identify programs based on our understanding of immunology and Physiocrine biology, we are unraveling the depth of this new biology in relation to T-cells and the molecular basis for orchestrating T-cells and other immune cell activity.

- ***Build a diverse biologics platform in immunology.*** We continue to deepen our expertise in protein production and develop biologic programs in three therapeutic modalities:
    1. Physiocrine natural protein therapy, as exemplified by Resolaris;
    2. Fc- Physiocrine fusion protein therapy, as exemplified by Stalaris; and
    3. A third therapeutic modality, in preclinical development, as exemplified by Project ORCA.
- ***Utilize our expertise in industry unique mechanisms and build our pipeline.*** With our therapeutically diverse pipeline, we can follow the science to create maximum value for the benefit of patients and may parlay different programs in business relationships to enable a diversity of commercialization channels, as well as potentially provide additional funding opportunities to partners outside of equity financings.
- ***Expand upon our knowledge and clinical experience with the Resokine pathway to address severe conditions characterized by immune imbalance.*** With Resolaris and Stalaris, we intend to target patients across diseases of different etiology with the commonality of immune imbalance at the level of the tissue. We believe that a protein therapeutic that promotes homeostasis without immunosuppression would have a unique and valuable competitive advantage across multiple disease settings.
- ***Leverage our exclusive worldwide commercial rights to our product candidates to form meaningful strategic partnerships to enhance our future development and commercial efforts.*** We aim to independently develop and commercialize our product candidates in areas that create value while balancing resource considerations. In parallel, we will pursue and evaluate, and may selectively form business relationships, to strategically accelerate and advance our programs through the expertise of or funding from the appropriate partners.
- ***Expand our intellectual property position in Physiocrine biology***. We intend to leverage our leadership position in this field to broaden our intellectual property positions in both the programs we advance and programs in development.
- ***Build a world class organization oriented to patients and focused on rigorous scientific, clinical and industrial advancements***. We continue to assemble a world class team with industry-recognized expertise in biology, medicine and the commercialization of innovative and important therapeutics. We intend to expand our relationships with key opinion leaders, patient advocacy groups and other business partners, and to solicit input from payors and others in the healthcare industry, to identify and develop our product opportunities and to design our development programs in order to maximize the availability of our product candidates to patients.

Harnessing the Power of Immunology with Physiocrine Biology

Overview

Physiocrines are proteins derived from the extracellular signaling regions or alternatively spliced variants of tRNA synthetases that modulate a range of cellular activities to maintain homeostasis. The term Physiocrines; *physio* for life and *crine* for specific activity, includes tRNA synthetase gene derived proteins which mediate nontranslational, extracellular functions. tRNA synthetases were once generally thought to only play a role in protein synthesis by catalyzing the aminoacylation of tRNAs to their respective amino acids. In 1999, Paul Schimmel, Ph.D. and colleagues discovered that a protein derived from one of the genes for tRNA synthetases could act as an extracellular modulator of angiogenesis. Since then, we and other researchers have verified that tRNA synthetase gene products may have a number of functional roles outside of protein synthesis mediated by extracellular signaling regions and multiple splice variants of aminoacyl tRNA synthetases. Those functional roles include immune modulation.

aTyr Pharma was founded based on the therapeutic potential of these extracellular regions of tRNA synthetases to restore health to tissues out of balance.

For over four billion years, the core function and structure of tRNA synthetases for protein synthesis remain primarily unchanged in most organisms. However, as organisms became more complex, changes in DNA sequences appeared in tRNA synthetase genes. These DNA mutations resulted in additional protein domains that are predicted to have important functions outside of protein synthesis. When released, we reason Physiocrines exert homeostatic and developmental control in many cell types, tissues, and organs and have been shown to play a role in regulation of glucose metabolism, organogenesis, angiogenesis, inflammation, cell death, stress responses that may lead to tumorigenesis, modulation of the immune response, mammalian target of rapamycin (mTOR) signalling, as well as interferon gamma (IFN-γ) and p53 signalling.

The Promise of Physiocrine-Based Medicines in Promoting Homeostasis

Homeostasis, or the coordinated regulation of tissues within the body, enables overall health and survival of an organism. For the complicated lives of multicellular organisms that have multiple organ systems, homeostasis represents a primal set of processes to enable life and combat damage and disease. Disruption of homeostasis can lead to disease and death. The concept of homeostasis was first described in 1865 by the French physiologist Claude Bernard, and Walter Cannon later coined the term. In the 150 years since this discovery, many proteins associated with homeostatic pathways have been discovered, ranging from insulin to erythropoietin.

Using our knowledge of bioinformatics, sequencing, proteomics and structural biology, we identified Physiocrines, a novel class of proteins that are present as biologically active signaling proteins derived from tRNA synthetase genes, an ancient gene family. We believe that Physiocrines are involved in orchestrating homeostatic activities to help the body restore diseased or damaged tissue to a healthier state. We observed that certain Physiocrines exhibit previously undescribed extracellular activities that are involved in restoring and regulating tissues to promote health. We believe that physiological perturbations, such as stress or changes in physiological state, alter or induce the release of Physiocrines from cells or platelets in the human body.

We expressed and purified over 200 Physiocrine regions across the family of 20 tRNA synthetase genes and evaluated these purified Physiocrines in numerous cell-based assays to determine their activity in several important human physiological pathways. Some of the data were published in July 2014 in *Science*, with the data categorized according to important areas of biology. This research revealed that there are approximately 100 Physiocrines with demonstrated activity in various cell-based assays related to immunological pathways. The specific regulatory capability of Physiocrines makes this class of proteins potential candidates for multiple therapeutic applications including rare diseases with an immune component, auto-immune disorders, neuro-degeneration, fibrosis and oncology.

Understanding and Harnessing Immunology Systems with Physiocrine Biology

We focus on understanding immunological pathways, using our knowledge of Physiocrine biology, to develop therapies for severe disease where we can achieve a transformative impact on a patient's life. We selected immunology as our initial area of focus for the following reasons:

- We believe immunology plays a significant role in most diseases, including rare genetic diseases;
- A number of Physiocrines have been shown to be differentially expressed by cells important for immune function;
- A large number of Physiocrine pathways appear to relate to immunology;
- Approximately 100 Physiocrines have demonstrated activity in various cell-based assays related to immunological pathways; and
- Potential therapeutic applications include rare diseases with an immune component, auto-immune disorders, neuro-degeneration, fibrosis and oncology.

We focus on modulators of immune processes for indications that represent severe, rare diseases, particularly genetically based diseases, because:

- Our scientific understanding of Physiocrines as potential immuno-modulators that intersected with multiple rare diseases;
- Patients with rare genetic diseases often face challenges related to the responses of their immune system to changes in tissues that are caused by their genetic mutations; and
- Pathological immuno-phenotypes in rare diseases present an opportunity for us to therapeutically intervene with greater impact.

Advantages of Physiocrine-Based Therapeutics

We believe that Physiocrines modulate the immune system and control or reduce tissue damage while maintaining the immune system's activity against exogenous pathogen based insults, and may possess the following advantages over most current immunological based drugs:

- As proteins designed by nature to control the immune system, Physiocrines may provide a unique mechanism to improve patient outcomes through their activity in either a single pathway or multiple pathways;
- Physiocrines possess the potential to control the immune system across multiple pathways at the level of an immune cell, rather than lowering the levels of a single immune protein;
- Physiocrines may potentially act as agonists at the level of the immune cell to reduce pro-inflammatory effects and induce resolution of inappropriate immune activity or inflammation;
- The therapeutic effects of Physiocrines may persist even after the Physiocrines have been cleared from circulation; and
- Resolaris, our first Physiocrine-based therapeutic candidate, has not demonstrated signs of general immunosuppression in the clinic, which represents a potential competitive advantage as compared to other immune agents that are often broadly immunosuppressive.

The Resokine Pathway – Modulating the Immune System

Overview of the Resokine Pathway

Our scientists were the first to discover the Resokine pathway (*reso* for restoring tissue health and *kine* for activity related to cytokines), an extracellular pathway involving human skeletal muscle tissue and arising from the activity of various regions of the protein histidine aminoacyl tRNA synthetase (HARS) encoded by its gene. We believe the Resokine pathway (i) is a homeostatic pathway that controls the set point of T-cells in the immune system to ensure appropriate control of immune responses, and (ii) may play an important role in muscle and lung health. We believe the Resokine pathway is characterized by:

- A series of Physiocrine proteins arising from a single gene, HARS;
- Balancing of the immune responses to promote homeostasis; and
- Disruptions or insufficiencies in the Resokine pathway in relation to disease perturbations at the level of the tissue lead to inappropriate immune responses contributing to disease.

Identification of the Resokine Pathway through In Vivo Screening Approaches

Our scientists discovered the Resokine pathway in human skeletal muscle using our *in vivo* screening systems in models of severe inflammation, combined with our knowledge of the effects of antibody binding to a specific tRNA synthetase in a population of patients with a particular rare myopathy and interstitial lung disease (ILD). The Resokine pathway encompasses physiological activities, including potential immuno-modulatory and other muscle health activities, arising from various Physiocrine regions of HARS. Animal studies and human pathophysiological data have shown that antibody-based blockade of the Resokine pathway may lead to muscle tissue deterioration and immune cell invasion.

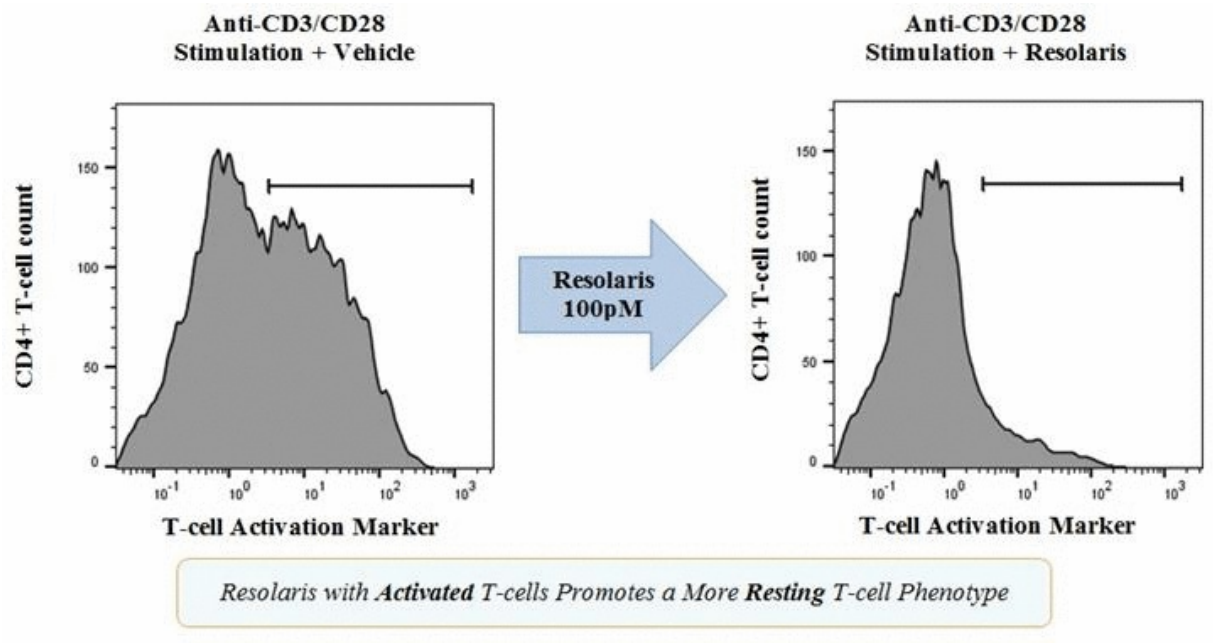
First Demonstration of a Splice Variant of HARS as an Immuno-modulator

We conducted *in vivo* screening activities of a splice variant from HARS, which we refer to as the immuno-modulatory domain or iMod domain, that we identified in our deep sequencing studies. For our studies of the iMod domain, we selected a rodent model of severe immune cell activity or inflammation induced by the administration of trinitrobenzene sulfonic acid, or TNBS, in which the inflammation is thought to be driven by excessive T-cell involvement in the gut, leading to the death of the study animals. Animals administered the iMod domain survived longer than those given either the vehicle control phosphate buffer solution, or PBS, or an approved drug control (Budesonide) ($p<0.01$), demonstrating the potential activity of the iMod domain as an immuno-modulator of excessive T-cell involvement.

Mechanism of Action

The Resokine pathway includes interactions with activated T-cells. Our scientists continue to elucidate the role of the Resokine pathway in affecting the level of activation of T-cells stimulated by CD3 and CD28. Our first two product candidates, Resolaris and Stalaris, harness the Resokine pathway and interact with T-cells to ‘place a brake’ on T-cell activation.

In vitro T-cell modulation experiments have demonstrated that at 100 pM Resolaris results in significant reduction of T-cell activation as shown by reduced expression of T-cell activation markers. Resolaris appears to work on *activated* T-cells by conferring characteristics closer to that of resting T-cells.



On the Left: CD4+ T-cells. 24 hour stimulation with anti-CD3/CD28 antibodies in the presence of vehicle.
On the Right: CD4+ T-cells. 24 hour stimulated with anti-CD3/CD28 antibodies in the presence of Resolaris.

Evidence of the Role of the Resokine Pathway in Rare Muscle and Lung Diseases

In 1983, Matthews and Bernstein published in *Nature* the observation that patients with a rare myopathy possessed antibodies to a single tRNA synthetase, HARS. Since then, it has been observed that patients with auto-antibodies to HARS (but not antibodies to the other 19 tRNA synthetases in the same patients) can develop both a debilitating myopathy characterized by weakness and skeletal muscle loss, as well ILD, both of which are characterized by T-cell invasion into diseased tissues. Numerous research laboratories have verified the existence of human anti-HARS antibodies, also known as Jo-1 antibodies, as one of the manifestations of the auto-immune disease, anti-synthetase syndrome.

Based on these observations, we chose to study the potential link between HARS antibodies and muscle disease in anti-synthetase syndrome patients with Jo-1 antibodies. Our scientists obtained serum samples from 18 of these patients to determine whether the Jo-1 antibodies specifically bound to the iMod domain. We determined that in each of the 18 Jo-1 antibody positive patients studied, a significant portion of Jo-1 antibody binding was to the iMod domain, compared to binding to other regions of HARS. We believe that in these patients, the binding of Jo-1 antibodies to the iMod domain blocked the immuno-modulatory properties of the iMod domain, therefore contributing to their myopathy and ILD. Independent laboratories have also observed in unrelated studies that the iMod domain is the primary antibody binding region in Jo-1 antibody patients with anti-synthetase syndrome.

Product Development Programs

Our Industry Unique Pipeline—A New Set of Potential Treatment Mechanisms for Patients

We believe that, as the first and only company engaged in the clinical development of therapeutics based on Physiocrine biology, we are positioned to develop and commercialize a pipeline based on a novel class of protein therapeutics that modulate important physiological processes. These agents are protected by intellectual property rights that we own or exclusively license. Below are summaries of our product development pipeline:

Programs	Development Status	Therapeutic Area
Resolaris	Phase 1b/2	Limb-Girdle Muscular Dystrophy (LGMD)
	Phase 1b/2	Early Onset Facioscapulohumeral Muscular Dystrophy
	Phase 1b/2	Facioscapulohumeral Muscular Dystrophy (FSHD)
	Under Evaluation	Duchenne Muscular Dystrophy (DMD)
Stalaris	Phase 1 in 2H 2017	Interstitial Lung Disease with an Immune Component
Project ORCA	Preclinical	3rd Therapeutic Area

Resolaris – Natural Protein Therapy Candidate

Overview

We created Resolaris to serve as a potentially first-in-class intravenous protein therapeutic for the treatment of rare myopathies with an immune component. We derived Resolaris from a naturally occurring protein, HARS, which we believe possesses the potential to reset the immune system in diseased tissue to a more normal state without general immunosuppression. Resolaris is released *in vitro* by human skeletal muscle cells. Resolaris may provide therapeutic benefit to patients in rare myopathy indications characterized by excessive immune cell involvement, particularly a type of T-cell known as CD8-T-cells, and macrophages. Immune cell invasion can cause and exacerbate muscle damage and stress. For example, CD8-T-cells have been observed to contribute to muscle damage by the release of proteins that destroy or damage skeletal muscle cells.

Resolaris

Wild-type human histidyl-tRNA synthetase (HARS) slightly truncated

To date, we have focused our clinical development of Resolaris on two broad types of rare genetic myopathies: FSHD and LGMD. DMD is another example of a rare myopathy with an immune component which might warrant clinical investigation. These particular myopathies represent several distinct, genetic sub-type indications that we believe Resolaris has the potential to treat. In each of these indications, skeletal muscle tissue exhibits dysfunction and becomes subject to immune cell invasion, which contributes to loss of function and deterioration of muscle tissue. These patients generally present with three common characteristics:

- expression of aberrant protein (in case of genetically based rare myopathies);
- immune cell invasion; and
- muscle cell damage and deterioration.

The Role of Immuno-Modulation in Rare Genetic Myopathies with an Immune Component

In normal muscle, muscle mass and function require a balance between muscle cell stress and damage and muscle cell regeneration and growth. The immune system helps maintain this balance by "cleaning up" damaged muscle cells after muscle damage and during the healing process. In rare myopathies, the balance is tipped to favor chronic pathophysiological muscle deterioration and persistent immune cell invasion. In genetically based rare myopathies, aberrant protein expression often occurs, as in the case of FSHD, LGMD, and DMD patients. *In vivo* rodent models of skeletal muscle deterioration and immune cell invasion have shown that Resolaris can combat both immune cell invasion into the muscle as well as muscle deterioration.

We intend to harness the body's power to restore skeletal muscle after stress or damage in the development of Resolaris for rare myopathy patients who have limited or no approved treatment options. Resolaris may offer a potential multi-pharmacologic therapeutic, synergistically modulating multiple pathways important to muscle health.

About Limb Girdle Muscular Dystrophy (LGMD)

LGMD refers to a group of rare genetic myopathies, of which there are more than 20 different subtypes, none with approved therapies. These myopathies are uniformly progressive and characterized predominantly by proximal weakness affecting the pelvic and shoulder girdles and usually sparing the face.

LGMD2B, a recessively inherited LGMD, is often termed dysferlinopathy, given that the causative mutations reside within the dysferlin gene. Patients experience progressive debilitating muscle weakness and atrophy as well as immune cell invasion in the skeletal muscle. There are multiple lines of evidence supporting a prominent role of inflammation in the pathophysiology of LGMD2B. Patients with LGMD2B possess a dysregulated immune response, including immune cell infiltration into affected muscle, increased expression of pro-inflammatory cytokines and altered cellular responses.

Based on a prevalence rate of 1:20,000, we estimate that LGMD affects an estimated 16,000 patients in the U.S., approximately 3,000 of whom have LGMD2B.

The FDA granted Resolaris (ATYR1940) fast track designation for the treatment of LGMD2B and orphan drug designation for the treatment of LGMD. The European Commission also granted orphan medicinal product designation for Resolaris (ATYR1940) for the treatment of LGMD.

About Facioscapulohumeral Muscular Dystrophy (FSHD)

FSHD is a rare genetic myopathy affecting an estimated 19,000 people in the United States for which there are no approved treatments. It is caused by a toxic gain of function in the DUX4 gene. The primary clinical phenotype of FSHD is debilitating skeletal muscle deterioration and weakness. The symptoms of FSHD often appear early in the face, shoulder blades, upper arms, lower legs and trunk, and can affect certain muscles while adjacent muscles remain healthy. In addition to muscle weakness, FSHD patients often experience debilitating fatigue and chronic pain. The disease is typically diagnosed by the presence of a characteristic pattern of muscle weakness and other clinical symptoms, as well as through genetic testing.

While FSHD can manifest at any age, the onset of symptoms in many patients occurs before the age of 18. We refer to this patient population as early onset FSHD. Within the early onset population are individuals with symptom onset at less than five years of age, with progression in disease prior to age ten. These individuals have generally the most severe muscle symptoms and extra-muscular manifestations such as auditory deficits and retinal complications that may result in vision loss. This sub-group of early onset patients are often referred to as having "infantile onset" FSHD. Estimates of prevalence vary; however, we believe the "infantile onset" FSHD population is approximately 1,000 in the U.S.

The FDA granted Resolaris (ATYR1940) fast track designation and orphan drug designation for the treatment of FSHD. The European Commission granted orphan medicinal product designation for Resolaris (ATYR1940) for the treatment of FSHD.

About Duchenne Muscular Dystrophy (DMD)

DMD is the most common fatal genetic disorder diagnosed in childhood, affecting approximately 1 in every 3,500 live male births (about 20,000 new cases each year worldwide). Because the Duchenne gene is found on the X-chromosome, it primarily affects boys across all races and cultures. DMD results in progressive loss of strength and is caused by a mutation in the gene that encodes for dystrophin. Because dystrophin is absent the muscle cells are easily damaged. The progressive muscle weakness leads to serious medical problems particularly issues related to the heart and lungs. Young men with DMD typically live into their late twenties. Although there are medical treatments that may help slow its progression, there is currently no cure for DMD in any of the over 50 genetic forms.

Recently, the FDA approved deflazacort, a steroid which acts as an immunosuppressive, for the treatment of DMD. DMD patients are characterized by immune dysregulation including increases in CD8 T-cell infiltration, macrophage infiltration, matrix metallopeptidase 9, tissue inhibitor of metalloproteinase-1, and tumor necrosis factor alpha. However, deflazacort also has negative effects on muscle cell biology. We believe a treatment that can modulate the immune system without causing immunosuppression and negative effects on muscle cell biology could potentially provide a benefit to these patients above and beyond standard of care.

We are currently evaluating DMD as a potential RMIC indication for future investigation with Resolaris.

Clinical Development

The following table summarizes our clinical trials to date:

Study ID / Status	Study Population	Number of Subjects	Phase	Study Design	Dosing Regimen	Dosing Duration
ATYR1940-C-001 ("001 Study") Completed	Healthy Subjects	32	1	Placebo Controlled, Randomized (3:1), Single Ascending Dose Safety Study	Single dose of 0.1 mg/kg, 0.3 mg/kg, 1.0 mg/kg, 3.0 mg/kg	Single dose with six subjects in each of the four dose cohorts
ATYR1940-C-002 ("002 Study") Completed	Adult FSHD	20	1b/2	Placebo Controlled, Randomized (3:1), Multiple Ascending Dose Safety Study	Weekly doses of 0.3 mg/kg (Cohort 1) Weekly doses of 1.0 mg/kg (Cohort 2) Weekly doses of 3.0 mg/kg (Cohort 3)	4 weeks (Cohorts 1 & 2) 12 weeks (Cohort 3)
ATYR1940-C-003 ("003 Study") Enrollment closed	Early Onset FSHD	8	1b/2	Open-Label, Intra-Patient Dose Escalation Study	Weekly doses starting at 0.3 mg/kg with potential dose escalation up to 3.0 mg/kg	12 weeks Trial concluding in the first half of 2017
ATYR1940-C-004 ("004 Study") Completed	LGMD2B and FSHD	18	1b/2	Open-Label, Intra-Patient Dose Escalation Study	Weekly and twice weekly doses starting at 0.3 mg/kg with potential dose escalation up to 1.0 mg/kg and 3.0 mg/kg	12 weeks
ATYR1940-C-005 ("005 Study") Enrollment closed	Adult FSHD from 002 Study	9	1b/2	Open-Label Safety Extension Study	Weekly doses of 3.0 mg/kg	Trial concluding in the first half of 2017
ATYR1940-C-006 ("006 Study") Enrollment closed	Adult LGMD2B, Adult FSHD, Early Onset FSHD from 003 & 004 Studies	8	1b/2	Open-Label Safety Extension Study	Weekly doses of 3.0 mg/kg	Trial concluding in the first half of 2017

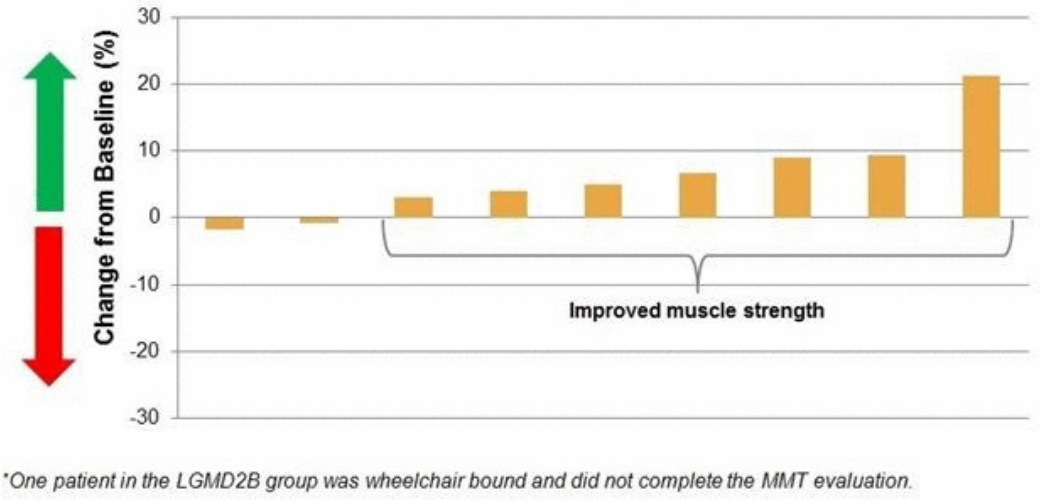
The planning and design of our exploratory Phase 1b/2 trials were guided by principles related to safety and tolerability. In particular, the trials were designed to evaluate the safety, tolerability, immunogenicity and pharmacokinetic (PK) profile of Resolaris in patients with adult FSHD, adult LGMD2B or early onset FSHD (as set forth in the table above). In addition, the studies also evaluated certain clinical assessments and the utility of exploratory pharmacodynamic (PD) markers (including MRI measurements to quantitate areas of potential muscle inflammation). The studies were not powered to demonstrate statistically significant evidence of therapeutic utility or a specific activity endpoint.

As part of clinical assessments in these studies, manual muscle testing (MMT), a validated assessment tool that measures muscle strength, was performed across 14 selected muscle groups at different time points in the study. Muscles are scored individually and a composite score is calculated. Progression of disease leads to lower scores and a negative change from baseline. Conversely, improvement in muscle function is indicated by higher scores and a positive change from baseline. In addition, a validated patient reported outcome measure designed specifically for neuromuscular disease, the individualized neuromuscular quality of life (INQoL) questionnaire, was utilized. FSHD and LGMD2B are progressive muscle diseases and we expect that an increase in disease burden would be reflected in decreased MMT and increased INQoL measurements over time.

Adult Patients with LGMD2B

Composite MMT scores increased over the course of the three month 004 Study for 78% of the LGMD2B patients (seven of nine). One patient could not complete the full MMT assessments at baseline and therefore the patient's scores were not recorded. Overall, the LGMD2B patients had a mean increase of MMT scores from baseline of 6.2%. Overall INQoL scores were relatively stable with approximately equal proportions of patients with decreases in disease burden compared to increases in disease burden.

Percentage Change From Baseline to Week 14 in Manual Muscle Test Composite Score by Patient (n=9*):



*One patient in the LGMD2B group was wheelchair bound and did not complete the MMT evaluation.

Patients with Early Onset FSHD

We are conducting an international, multi-center, open-label, intra-patient, placebo run-in, dose escalation Phase 1b/2 clinical trial (003 Study) designed to evaluate the safety, tolerability, immunogenicity and exploratory assessments of clinical activity of Resolaris at weekly doses of 0.3, 1.0 and 3.0 mg/kg in patients with early onset FSHD for a total of 12 weeks.

We have completed the first stage of this trial and expect to announce top-line results and conclude the trial in the second quarter of 2017.

An interim data review was conducted for the first four early-onset FSHD patients that completed treatment with Resolaris (age range of 16 to 20). Patient's INQoL scores were relatively stable with two patients demonstrating slight decreases in disease burden and one patient with an increase. The fourth patient did not have a baseline INQoL assessment and was excluded from the analysis. Muscle strength, as noted by MMT scores, increased over the course of the three month trial for 75% of the early onset patients (three of four). Overall, the early onset FSHD patients had a mean increase of MMT scores from baseline of 6.7%.

Adult Patients with FSHD

We have conducted four trials which included adult FSHD patients, including our 002 Study, an international Phase 1b/2 placebo-controlled clinical trial; our 004 Study, an international Phase 1b/2 open-label, intra-patient, placebo run-in, dose escalation clinical trial, our 005 Study, a long-term safety extension clinical trial with patients rolling over from our 002 Study, and our 006 Study, a long-term safety extension clinical trial with patients rolling over from our 004 Study.

We announced data during 2016 from three separate clinical trials treating adult FSHD patients with Resolaris: our 002 Study, 004 Study and our 005 Study. While these were distinct trials under separate protocols and were not designed for comparability, based on data previously disclosed, an increase in MMT scores was observed in approximately 50% of patients across these three separate studies. In the placebo-controlled 002 trial, a trend in improvement in MMT scores for patients treated with Resolaris was observed compared with placebo patients, with a concentration of improved MMT scores in the upper limbs. For the eight FSHD patients in the 004 Study, the overall MMT scores were relatively stable with four of the eight patients presenting with a slight increase in their muscle strength.

In addition, disease burden, as measured by the INQoL assessment, was lower in a majority of FSHD patients treated with Resolaris across our three separate studies. Patients treated with Resolaris showed an improvement, as assessed by INQoL, compared with placebo, and we observed the greatest improvement in patients in Cohort 3 (3.0 mg/kg for 12 weeks) of the 002 Study, a placebo-controlled trial. Patients in Cohort 3 reported approximately 9.9% improvement in INQoL compared with approximately 15.6% worsening in the placebo group at week 14. Five out of the six patients dosed with Resolaris in Cohort 3 showed overall improvement in their INQoL score at week 14, versus zero out of two patients on placebo.

Biomarkers

A number of exploratory PD markers and clinical assessments were conducted to better understand their utility in FSHD and LGMD2B. Various exploratory biomarkers (including targeted muscle T2 and STIR MRI and various plasma proteins) did not generally establish sufficiently high or consistent levels or robust signals across a sufficient number of patients to determine test article effects. Peripheral cell based biomarkers will be assessed in the future using one or more mechanistic assays currently under development for agonists of the Resokine pathway and T-cell activity. Future trials will be designed using one or more of these mechanistic assays, as well as the option to assess local immune components in skeletal muscle directly with biopsies. Targeted muscle T2/STIR MRI will not be prioritized as a biomarker in the near-term.

Long-Term Safety Extension Studies in Patients with Adult FSHD, Adult LGMD2B, and Early Onset FSHD (005 and 006 Studies)

These ongoing international, multi-center, open-label extension clinical trials are designed to assess the long-term safety, effects on biomarkers and systemic exposure of Resolaris in patients with adult FSHD, adult LGMD2B, and early onset FSHD from our 002, 003 and 004 Studies. Patients receive weekly doses of 3.0 mg/kg on an ongoing basis. We provided an update from the 005 Study in December 2016 and plan to provide an update from the 006 Study in the middle of 2017. We are currently in the process of concluding both of these studies as we believe the studies have met their objectives to evaluate the safety, tolerability and immunogenicity of Resolaris in patients from our 002, 003 and 004 Studies.

Safety and Tolerability Profile

Our early clinical development plan for Resolaris evaluated three rare genetic myopathies: adult FSHD, early onset FSHD, and LGMD2B where there is no therapeutic standard of care. This allowed us to collect important information related to the safety, tolerability and immunogenicity of our first Physiocrine in the clinic. Establishing a safety dossier in our Phase 1b/2 trials in treatment naïve patients was an important developmental milestone for us to achieve before evaluating whether to broaden our indication potential for Resolaris.

As of December 31, 2016, 44 patients and 24 healthy volunteers have received Resolaris across all trials for a total drug exposure of 191 months. In those trials, Resolaris was well tolerated in all doses tested, across various age groups, and with long-term exposure. No serious adverse events were reported by the study investigators. A low incidence of adverse events were reported in these trials and all adverse events were mild-to-moderate in intensity. There were no observed signs of general immunosuppressive effects which is consistent with a homeostatic pathway working at the tissue level.

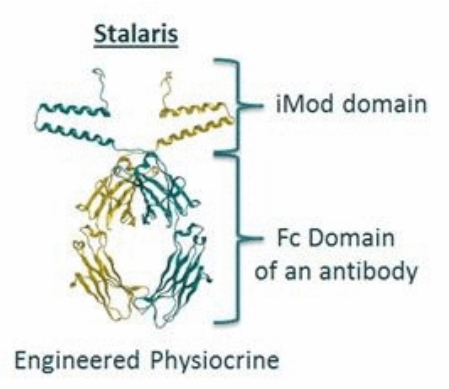
A low level of anti-drug antibody assay signals were observed in these trials. These signals did not reach levels to trigger a neutralizing assay and did not result in clinical symptoms.

Protocol discontinuations in these studies were primarily driven by mild-to-moderate transient infusion related reactions and elevations in a sponsor defined Jo-1 antibody level threshold. Discontinuation criteria in these trials related to infusion rate reactions and elevations in Jo-1 antibodies were implemented with a conservative approach as we gained understanding of this first Physiocrine in the clinic.

Stalaris – First Engineered Fusion Protein of a Physiocrine

Overview

To leverage our knowledge of the Resokine pathway, our scientists established a discovery program conducting a series of protein engineering experiments *in vivo* to enhance the activity of the iMod domain. The goal of the program was to develop a potential therapeutic that would retain only the N-terminal immuno-modulatory and fibro-modulatory activities of Resokine while enabling enhanced activity *in vivo* using a different dosing regime. Fc fusion proteins have been successfully commercialized previously by others to enhance exposure of a naturally occurring protein while enabling biological activity. We explored this approach by fusing the immunoglobulin Fc with one iMod domain, which can form a dimer. Enbrel, Orencia and Zaltrap are commercialized examples of immunoglobulin Fc fusion proteins.



Fc Fusion Platform

Our Fc fusion experiments have delineated how to enhance the exposure of the iMod domain of Resokine while maintaining activity and have provided insights into the immuno-modulatory activity of the iMod domain. Initial experiments have indicated that Fc fusion proteins can increase exposure and maintain iMod domain activity. Our efforts in this research program have led to the selection of our second product candidate, Stalaris. This fusion protein potentially represents a novel Fc-Physiocrine platform for future Physiocrine-based therapies.

Currently we are producing our Stalaris molecules in *E.coli* by expression in inclusion bodies and refolding to recreate the native structure. This is in contrast to some other marketed Fc fusion therapeutics that are manufactured in Chinese hamster ovary (CHO) cells, although the FDA-approved commercial product Romiplostim (NPlate) is also expressed in *E.coli* and refolded. We are working with a third party manufacturer on the development and GMP manufacturing process for the production of Stalaris preclinical and clinical drug substance.

Interstitial Lung Diseases (ILDs) and the Role of Immunology

The Resokine pathway may play an important role in maintaining lung health. We believe the Resokine pathway plays a role in the regulation of tissue homeostasis with respect to immune cell invasion and residence, including in lung tissue. Jo-1 antibody patients often develop ILD, a pathophysiologic state that involves inflammation and fibrosis of the alveoli, distal airways and septal interstitium of the lungs, includes various patterns of lung pathology and is associated with markedly impaired lung function. We have observed that Jo-1 antibodies isolated from these patients bind to the iMod domain that we believe harbors immuno-modulatory activity.

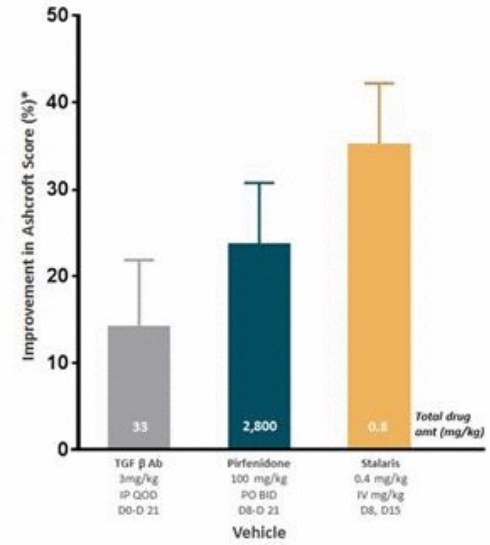
ILD develops in approximately 85% of anti-synthetase patients with Jo-1 antibodies to Resokine. It can include the presence of focal immune cell infiltrates and an acinar pattern of involvement on chest computed tomography (CT) scan, lymphocytic predominance on broncho-alveolar lavage and lymphocytic invasion of alveolar and interstitial lung tissues on biopsy, and can advance to fibrosis. The pathological patterns in Jo-1 antibody ILD include cellular and fibrotic forms of non-specific interstitial pneumonitis, usual interstitial pneumonitis and diffuse alveolar damage. The development of ILD in Jo-1 antibody patients, particularly the acute severe forms of the disease, portends high morbidity and mortality. Elevations in a number of circulating immune proteins are observed in Jo-1 antibody associated ILD including interferon (IFN)-inducible chemokines CXCL9, or MIG, and CXCL10 or IP-10, IL-8 and IL-6.

ILD occurs in other settings such as rare genetic disorders, environmental exposures, as a side effect of certain therapeutics and as a manifestation of certain connective tissue disorders. Among these forms of ILD, we have identified several that result in severe and progressive lung disease and share immune-pathophysiology features that have the potential to be impacted by our demonstrated Stalaris activities. Examples of rare pulmonary diseases with an immune component include idiopathic non-specific interstitial pneumonias, idiopathic pulmonary fibrosis, lymphocytic interstitial pneumonia, bleomycin (the chemotherapeutic agent)-induced pulmonary fibrosis, and ILD in the setting of systemic sclerosis, or scleroderma, and sarcoidosis.

Preclinical Development

To test our hypothesis that augmenting the Resokine pathway with Stalaris has therapeutic potential in ILD, we have generated data in a mouse model of lung inflammation and pulmonary fibrosis. Stalaris has also shown promising therapeutic activity in this bleomycin-induced model (as set forth in the table below) which has been used previously in the development of therapeutics for different forms of ILD, including the drug pirfenidone, or Esbriet, which was approved by the FDA in October 2014 for the treatment of idiopathic pulmonary fibrosis. We noted that Stalaris administration attenuated the radiographic and histological manifestations of pathophysiology in this model when it was dosed therapeutically. These mouse Stalaris pharmacology data, along with data discussed above delineating our immuno-modulatory activity in other settings, provide preclinical evidence supporting our hypothesis that augmenting the Resokine pathway has therapeutic potential in ILD.

Bleomycin Rodent Model for *Idiopathic Pulmonary Fibrosis* (IPF):



Project ORCA - Third Biologics Program

Based on our knowledge of Physiocrine biology, we have established a third biologics program from our research efforts, code name "Project ORCA," currently in preclinical development. Project ORCA represents a third therapeutic modality distinct from Resolaris or Stalaris.

Our Discovery Engine for Therapeutic Applications of Physiocrines in Immunology

We plan to leverage our discovery engine to identify other Physiocrine pathways of interest and select additional potential product candidates for preclinical and clinical investigation in a variety of disease settings. The engine that drives our discovery efforts is based on our scientific investigation of Physiocrine pathways and their proteins, coupled with a process of identifying disease indications that may benefit from a Physiocrine therapeutic. Through a combination of deep sequencing and bioinformatics panning, augmented by proteomic analysis, we have identified over 300 naturally occurring Physiocrines. We then expressed and purified over 200 of these Physiocrines. Our strategy for identifying function and potential indications begins with developing a series of phenotypic assays for *in vitro* and *in vivo* evaluations of function.

A key step in the discovery engine requires mining data from rare disease patients and linking this to the data generated in our phenotypic profiling experiments either *in vitro* or *in vivo* models of immunology. We believe our strategy of understanding Physiocrine function by using *in vivo* experiments early and often while using patient data to focus this *in vivo* exploration has been validated by our Resolaris, Stalaris and Project ORCA programs. Additionally, we believe our discovery engine can be applied to other members of the Physiocrine family to help identify additional indications that may benefit from therapeutic intervention with Physiocrines.

We believe the biology of Physiocrines presents a novel protein therapeutic development opportunity based on the modulation of important immunological pathways applicable to multiple diseases. This "pathway" approach or "physiology first" paradigm as we call it, which leverages the understanding of a basic physiological process, has been used successfully to create some of the most important therapeutics in such diverse areas as oncology and ophthalmology. Given the breadth of our discoveries, we currently focus on Physiocrine pathways related to immune and regeneration responses to explore for product candidates with rare disease applications.

Competition

The biotechnology and pharmaceutical industries are intensely competitive. We will face competition with respect to Resolaris and Stalaris and any other protein therapeutics we may develop or commercialize in the future from pharmaceutical companies, biotechnology companies and universities and other research institutions. Our competitors may have substantially greater financial, technical and other resources, such as larger research and development staff and experienced marketing and manufacturing organizations. Additional mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated in our competitors. Competition may increase further as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these industries. Our competitors may succeed in developing, acquiring or licensing on an exclusive basis drug products that are more effective or less costly than any product candidate that we may develop.

Although we believe we are the only company engaged in the discovery and development of therapeutics based on Physiocrine pathways, we are aware of other companies that are developing products that could compete as treatments for our targeted indications, as described below.

In the area of rare myopathies with an immune component, we expect to face competition from a number of companies, academic institutions and other organizations, including Sarepta Therapeutics, PTC Therapeutics, Inc., Marathon Pharmaceuticals, Santhera Pharmaceuticals, Italfarmaco S.p.A, Summit Therapeutics, Catabasis Pharmaceuticals, Inc., FibroGen, Inc., F. Hoffmann-La Roche AG, Bristol Myers Squibb, Milo Biotechnology, LLC, Nobelpharma Co. Ltd., Pfizer, Inc., and Ultragenyx Pharmaceuticals, that are engaged in the clinical development of therapeutics to address muscle loss and muscle weakness in a variety of indications. More specifically, in the area of LGMD, we are aware of a number of academic institutions engaged in the clinical development of therapeutics, including Genethon, a not-for-profit research laboratory created by the Association Française contre les Myopathies, or French Muscular Dystrophy Association, which has completed an experimental Phase 1 clinical trial in LGMD2C using gene therapy; Nationwide Children's Hospital, which is currently conducting a Phase 1/2a clinical trial of an AAV vector to transport the alpha-sarcoglycan gene into muscles in LGMD2D; and NeuroGen Brain and Spine Institute in India, which is currently conducting a Phase 1 clinical trial in an unspecified form of LGMD using stem cell therapy. In addition, Pfizer currently has a program Domagrozumab (PF-06252616) which is in Phase 1b/2 clinical trials for the treatment of LGMD2I as well as a Phase 2 program for DMD. In the area of FSHD, while there are currently no approved products for this disease, Acceleron Pharma Inc. is developing a clinical candidate, ACE-083, a locally acting protein therapeutic designed to increase muscle mass and strength in patients with neuromuscular disorders and other diseases characterized by a loss of muscle function, including FSHD in which it initiated a Phase 2 trial in the fourth quarter of 2016. In addition, Facio Therapies recently announced its plans to screen chemical libraries to identify chemical compounds that will boost the expression of proteins known to repress one of the causal genes responsible for FSHD. In the area of DMD, two therapies have been approved in the last 12 months: Exondys 51 from Sarepta and Emflaza from Marathon Pharmaceuticals. Marathon Pharmaceuticals and PTC Therapeutics, Inc. recently announced entering an asset purchase agreement whereby PTC Therapeutics, Inc. will acquire all rights to Emflaza. Exondys 51 is an antisense oligonucleotide indicated for the treatment of DMD in patients who have a confirmed mutation of the DMD gene that is amenable to exon 51 skipping. The approval is under accelerated approval based on an increase in dystrophin in skeletal muscle observed in some patients, but no clinical benefit has been established. Emflaza is a corticosteroid (deflazacort) indicated for the treatment of DMD in patients 5 years of age or older.

In the area of rare lung diseases with an immune component, notably ILD, we expect to face competition from pirfenidone, which is marketed by F. Hoffmann-La Roche AG, Shionogi Ltd. and Il Dong Pharmaceutical globally, as well as nintedanib, a small molecule tyrosine-kinase inhibitor marketed by Boehringer Ingelheim, both of which were approved by the FDA in October 2014. We are also aware of a number of companies engaged in the clinical development of therapeutics for lung diseases, including Astra Zeneca plc., Biogen Inc., Bristol-Myers Squibb, FibroGen, Inc., Asahi Kasei, Chiesi Farmaceutici S.p.A, Chugai, Promedior, Inc., Pliant Therapeutics, Inc. and Sanofi S.A.

Sales and Marketing

We intend, where strategically appropriate, to build the commercial infrastructure in the United States and Europe necessary to effectively support the commercialization of our product candidates, if and when we believe a regulatory approval of the first of such product candidates in a particular geographic market appears imminent. We may elect to utilize strategic partners, distributors, or contract sales forces to assist in the commercialization of our products in selected geographic locations or for particular indications.

The commercial infrastructure for products directed at rare disease indications typically consists of a targeted, specialty sales force that calls on a limited and focused group of physicians supported by sales management, medical liaisons, internal sales support, an internal marketing group, and distribution support. One challenge unique to commercializing therapies for rare diseases is the difficulty in identifying eligible patients due to the very small and sometimes heterogeneous disease populations.

Additional capabilities important to the marketing of therapeutics for rare diseases include the management of key accounts such as managed care organizations, group-purchasing organizations, specialty pharmacies, and government accounts. To develop the appropriate commercial infrastructure, we will have to invest significant amounts of financial and management resources, some of which will be committed prior to any confirmation that any of our product candidates will be approved.

Manufacturing

We currently contract with third parties for the manufacturing and testing of our product candidates for preclinical studies and clinical trials and intend to do so in the future. We do not own or operate manufacturing or testing facilities for the clinical or commercial production of our product candidates. We currently have no plans to build our own clinical or commercial scale manufacturing capabilities. The use of contracted development and manufacturing organizations, or CDMOs, and contract research organizations, or CROS, is cost-efficient and has eliminated the need for our direct investment in manufacturing facilities and additional resources early in development. Although we rely on CDMOs and CROs, we have personnel with extensive biologics development and manufacturing experience to oversee such CDMOs and CROs.

To date, our CDMOs and CROs have met our manufacturing requirements for clinical development and we expect that our current CDMOs and CROs are capable of providing sufficient quantities of our product candidates to meet our anticipated clinical development needs.

Resolaris

Resolaris is expressed in recombinant bacteria, purified, formulated, filled and packaged for clinical use. For our Phase 1b/2 clinical trials conducted to date, the drug substance for Resolaris was manufactured in India by Syngene International Limited, or Syngene. We have a non-exclusive license to the host-cell line used to produce drug substance for Resolaris at Syngene. Resolaris drug product for such Phase 1b/2 clinical trials was manufactured by CDMOs in India and the United States.

To meet our projected needs for future clinical trials and larger scale commercial manufacturing, we are working with Fujifilm Diosynth Biotechnologies USA, Inc., or Fujifilm, and have completed the development, scale-up and GMP manufacturing process for the production of Resolaris drug substance. We have also successfully demonstrated comparability of the product manufactured at the different scales and sites. The host-cell line used to produce the drug substance for Resolaris at Fujifilm is in Fujifilm's control. We have an option to obtain a non-exclusive license for such host-cell line if we move production to another CDMO. The drug product process for Resolaris was also successfully scaled and transferred to a CDMO in Germany.

We contract with CROs to conduct labeling, as well as for the storage and distribution of Resolaris to clinical sites. Additionally, we have negotiated with additional storage and labelling CROs to enable the commercial storage and supply of Resolaris.

Stalaris

Our second clinical candidate, Stalaris, is a Fc fusion molecule that is expressed in recombinant bacteria. Currently we are producing our Stalaris molecules in *E.coli* by expression in inclusion bodies and refolding to recreate the native structure. We are working with CDMOs in the United States on the development and GMP manufacturing process for the production of Stalaris preclinical and clinical drug substance and drug product. We have a non-exclusive license to the host-cell line used to produce drug substance for Stalaris. We intend to contract with CROs to conduct labeling, storage and distribution of Stalaris to clinical sites.

Patents and Proprietary Rights

We strive to protect the proprietary technologies that we believe are important to our business, including seeking and maintaining patent protection intended to cover the composition of matter of our product candidates, their methods of use, related technology and other inventions that are important to our business. We own, or have exclusive licenses to, over 175 issued patents or allowed patent applications with predicted expiration dates ranging from 2026 to 2034. In addition to patent protection, we also rely on trade secrets and careful monitoring of our proprietary information to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

Our success will depend significantly 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, maintain our licenses to use intellectual property owned by third parties, preserve the confidentiality of our trade secrets and operate without infringing the valid and enforceable patents and other proprietary rights of third parties. We also rely on know-how, continuing technological innovation and in-licensing opportunities to develop, strengthen, and maintain our proprietary position in the field of Physiocrine therapeutics.

A third party may hold intellectual property, including patent rights, which is important or necessary to the development of our products. It may be necessary for us to use the patented or proprietary technology of third parties to commercialize our products, in which case we would be required to obtain a license from these third parties on commercially reasonable terms, or our business could be harmed, possibly materially.

We plan to continue to expand our intellectual property estate by filing patent applications directed to new methods of treatment, therapeutics and additional new product forms thereof with new therapeutic or pharmacokinetic properties. Specifically, we seek patent protection in the United States and internationally for novel compositions of matter covering our protein therapeutics, next generation product forms and the use of these compositions in a variety of therapies.

The patent positions of biopharmaceutical companies like us are generally uncertain and involve complex legal, scientific and factual questions. In addition, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Consequently, we do not know whether any of our product candidates will be protectable or remain protected by enforceable patents. We cannot predict whether the patent applications we are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient proprietary protection from competitors. Any patents that we hold may be challenged, circumvented or invalidated by third parties.

Because patent applications in the United States and certain other jurisdictions are maintained in secrecy for 18 months, and since publication of discoveries in the scientific or patent literature often lags behind actual discoveries, we cannot be certain of the priority of inventions covered by pending patent applications. Moreover, we may have to participate in interference proceedings declared by the United States Patent and Trademark Office, or USPTO, or a foreign patent office to determine priority of invention or in post-grant challenge proceedings, such as oppositions, that challenge priority of invention or other features of patentability. Such proceedings could result in us incurring substantial costs, even if the eventual outcome is favorable to us.

The patent portfolios for our most advanced programs are summarized below.

Resolaris. Our Resolaris patent portfolio is comprised of a number of patent families and includes U.S. Patent No. 8,835,387, which issued on September 16, 2014 and is predicted to expire in 2033; and U.S. Patent No. 9,273,302, which issued on March 1, 2016 and is predicted to expire in 2033. This patent family is jointly owned by us and our 98% owned subsidiary, Pangu Biopharma. Patent applications in the same family as U.S. Patent No. 8,835,387 are pending in a variety of worldwide jurisdictions, including the United States, Australia, Brazil, Canada, China, Europe, India, Japan, Korea, Mexico, New Zealand, Russia and South Africa. The Resolaris patent portfolio also encompasses additional issued patents and pending patent applications that cover Resolaris and related proteins; these patents and patent applications are wholly owned by us. This second patent family includes U.S. Patent No. 9,127,268, which issued on September 8, 2015; European Patent No. 2509625, which granted on January 28, 2015; Japanese Patent No. 5819314, which granted on October 9, 2015; Chinese Patent No. ZL 201080061989.7, which granted on September 21, 2016; and Australian Patent No. 2010327926, which issued August 21, 2014, and related applications that are pending in the United States, Australia, Canada, Europe, China, Japan, and Hong Kong. Patents that issue from these applications, if any, are expected to expire in 2030 plus any patent term extension. Also included with the Resolaris patent portfolio are pending patent applications to specific methods of use of Resolaris and related proteins, and disease polymorphisms of HARS. These applications have been filed in the United States as U.S. provisional applications and in some cases under the Patent Cooperation Treaty, or PCT. U.S. provisional applications may be used to establish non-provisional U.S. applications, PCT applications and other national filings worldwide. PCT applications are eligible for filing in most worldwide jurisdictions, including the United States. If issued, these patents are predicted to expire between 2033 and 2034.

Stalaris. Our Stalaris patent portfolio, includes derivatives of Resokine, including the iMod domain, related splice variants, and next-generation product forms with modified therapeutic activity or pharmacokinetic characteristics, is comprised of a number of patent families and includes U.S. Patent No. 8,404,242, and U.S. Patent No 8,753,638, which issued on March 26, 2013 and June 17, 2014, respectively, and are expected to expire in 2031 and 2030. Also included in this patent family are Japanese Patent No. 5756751, which granted on June 5, 2015; and Australian Patent No. 2010226726, which issued on October 16, 2014. This patent family is jointly owned by us and our 98% owned subsidiary, Pangu Biopharma, and includes pending applications in United States, Australia, Canada, Europe, China, Japan, and Hong Kong. Patents that issue from these applications, if any, are expected to expire in 2030, plus any patent term extension. The Stalaris patent family also includes patent applications filed on related splice variants of HARS. This patent family includes applications that are pending in the United States, Australia, Canada, Europe, China, India, Japan, Korea, New Zealand, Russia and Hong Kong. This patent family is jointly owned by us and Pangu Biopharma. Also included within the Stalaris patent portfolio are pending applications to specific product forms of Stalaris, Resolaris and other HARS splice variants which include patent families to Fc fusion proteins, pegylated forms and variants with substituted D amino acids. These applications have been filed in the United States as U.S. provisional applications and in some cases under the PCT. If issued, these patents are predicted to expire between 2033 and 2034.

Our pipeline of Physiocrines is covered by a series of 21 patent families, which covers all 20 human cytosolic tRNA synthetases. At least 19 Physiocrine patents are issued in the United States, and applications are pending to the corresponding Physiocrine polynucleotide sequences. These cases are jointly owned by us and Pangu Biopharma, and include pending applications in the United States, Australia, Canada, India, Europe, China and Japan. Patents that issue from these applications, if any, would be expected to expire in 2031. Additional patent applications have also been separately filed on GARS (Glycyl-tRNA synthetase), DARS (Aspartyl-tRNA synthetase), YARS (tyrosyl-tRNA synthetase), and other tRNA synthetases, and any patents issuing from these patent applications would be expected to expire between 2026 and 2030. We have also exclusively in-licensed from TSRI, patents and patent applications related to YARS and specific monomeric forms of tRNA synthetases.

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 generally 20 years from the earliest date of filing the non-provisional patent application from which the patent issued.

In the United States, the patent term of a patent that covers a drug approved by the U.S. Food and Drug Administration, or FDA, may also be eligible for patent term extension, which permits patent term restoration 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. Patent 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. Similar provisions are available in Europe and other non-United States jurisdictions to extend the term of a patent that covers an approved drug. In the future, if and when our pharmaceutical products receive FDA approval, we expect to apply for patent term extensions on patents covering those products. We intend to seek patent term extensions to any of our issued patents in any jurisdiction where these are available, however there is no guarantee that the applicable authorities, including the FDA in the United States, will agree with our assessment of whether such extensions should be granted, and even if granted, the length of such extensions.

We also rely on trade secret protection for our confidential and proprietary information. Although we take steps to protect our proprietary information and trade secrets, including through contractual means with our employees and consultants, third parties may independently develop substantially equivalent proprietary information and techniques or otherwise gain access to our trade secrets or disclose our technology. Thus, we may not be able to meaningfully protect our trade secrets. It is our policy to require our employees, consultants, outside scientific collaborators, sponsored researchers and other advisors to execute confidentiality agreements upon the commencement of employment or consulting relationships with us. These agreements provide that all confidential information concerning our business or financial affairs developed or made known to the individual during the course of the individual's relationship with us is to be kept confidential and not disclosed to third parties except in specific circumstances. In the case of employees, the agreements provide that all inventions conceived by the individual, and which are related to our current or planned business or research and development or made during normal working hours, on our premises or using our equipment or proprietary information, are our exclusive property.

Research and License Agreements

The Scripps Research Institute

We are party to an amended and restated research funding and option agreement with The Scripps Research Institute, or TSRI. Under the agreement, we provide funding to TSRI to conduct certain research activities related to aminoacyl tRNA synthetases. The agreement renews automatically for successive 12 month periods starting on May 31 of each year unless we provide written notice of our desire to terminate the agreement at least 30 days prior to the end of the applicable 12-month period. Under the agreement, the parties agree to update the amount of annual funding for such successive 12-month periods as mutually agreed in good faith by the parties. We have the right to terminate the agreement at any time upon six months' written notice, and TSRI has the right to terminate the agreement if we fail to make any payment under the agreement within ten days of being notified by TSRI that such payment is overdue. Additionally, each party may terminate the agreement in the event of an uncured material breach by the other party or for insolvency of the other party.

Under the amended and restated research funding and option agreement, TSRI has granted us options to enter into license agreements to acquire rights and exclusive licenses to develop, make, have made, use, have used, import, have imported, offer to sell, sell and have sold certain licensed products, processes and services based on certain technology arising from the sponsored research activities. Pursuant to the terms of these license agreements, TSRI is entitled to receive tiered royalties as a percentage of net sales, ranging from the low to mid-single digits, with these royalty rates subject to increase if we challenge the validity or enforceability of any of the licensed patent rights under certain circumstances. The royalty rates are subject to reduction to the extent we need to obtain any rights from third parties to make, use, or sell the licensed products, processes or services, subject to a minimum floor in the single digits. Additionally, we have agreed to pay TSRI a percentage of non-royalty revenue we receive from our sublicensees or partners, with the amount owed decreasing if we enter into the applicable sublicense or partnering agreement after meeting a specified clinical milestone. In addition, we are obligated to make payments to TSRI of up to an aggregate of $2.75 million under each license agreement upon the achievement of specific clinical and regulatory milestone events.

Under the terms of the license agreements, we are obligated to use commercially reasonable efforts and diligence to develop and commercialize licensed products, processes and services and to obtain regulatory approvals as necessary.

We may terminate the license agreements upon mutual agreement with TSRI or unilaterally upon 90 days' notice, and TSRI has the right to terminate the agreements under certain circumstances, including our uncured material breach of the agreements and if TSRI determines that we are not engaged in research, development, manufacturing, marketing or sublicensing activities reasonably appropriate to put the licensed patents into commercial use, and to make the licensed subject matter reasonably available to the public, in the countries covered by the license.

Pangu Biopharma

In October 2007, we formed our Hong Kong subsidiary, Pangu BioPharma Limited, or Pangu BioPharma, a company registered in Hong Kong, to collaborate with the Hong Kong University of Science and Technology, or HKUST, on the discovery and development of aminoacyl tRNA synthetase protein therapeutics. We hold 98% of the outstanding shares of Pangu BioPharma, and a subsidiary of HKUST holds the remaining outstanding shares. Beginning in July 2008, Pangu BioPharma, in collaboration with HKUST, entered into a series of three research grant agreements with the Government of the Hong Kong Special Administrative Region to carry out research in the discovery and development of Physiocrines. In December 2016, Pangu BioPharma renewed its annual joint research agreement with a subsidiary of HKUST, under which Pangu BioPharma agrees to fund research to be performed in 2017 under the agreement by the subsidiary of HKUST with respect to development of aminoacyl tRNA synthetase protein therapeutics. Pangu BioPharma is the sole beneficial owner of all resulting intellectual property rights from the research performed under these agreements, subject to the right of HKUST's subsidiary to use certain background intellectual property of HKUST in conducting the research and, in the event Pangu BioPharma applies for individual funding of any work under the research programs, compliance with the terms and conditions of any written agreement covering ownership of such funded works. Pangu BioPharma funds the annual research on a quarterly basis. Either party may terminate the agreement during the annual period upon an uncured breach of the agreement by the other party. We are also party to a license agreement with Pangu BioPharma, pursuant to which Pangu BioPharma has granted us an exclusive, royalty-bearing license (with a right to sublicense) in and to certain of Pangu BioPharma's solely and jointly owned patent rights and know-how to research, develop, manufacture, use, import, export, distribute, offer for sale, sell and have sold products incorporating such patent rights and know-how for any therapeutic, prognostic or diagnostic use throughout the world.

Government Regulation

Government authorities in the United States, including federal, state, and local authorities, and in other countries, extensively regulate, among other things, the manufacturing, research and clinical development, marketing, labeling and packaging, storage, distribution, post-approval monitoring and reporting, advertising and promotion, and export and import of pharmaceutical and biological products, such as those we are developing. Pricing of such products is also subject to regulation in many countries. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local, and foreign statutes and regulations require the expenditure of substantial time and financial resources.

U.S. Government Regulation

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and its implementing regulations, and biologics under the FDCA and the Public Health Service Act, or PHSA, and its implementing regulations. FDA approval is required before any new unapproved drug or biologic or dosage form, including a new use of a previously approved drug, can be marketed in the United States. Drugs and biologics are also subject to other federal, state, and local statutes and regulations. If we fail to comply with applicable FDA or other requirements at any time during the product development process, clinical testing, approval process or after approval, we may become subject to administrative or judicial sanctions. These sanctions could include the FDA's refusal to approve pending applications, license suspension or revocation, withdrawal of an approval, untitled or warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties or criminal prosecution. Any FDA enforcement action could have a material adverse effect on us.

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

- completion of extensive preclinical laboratory tests and preclinical animal studies, all performed in accordance with the Good Laboratory Practices, or GLP, regulations;
- submission to the FDA of an investigational new drug application, or IND, which must become effective before human clinical trials may begin and must be updated annually;
- approval by an independent institutional review board, or IRB, or ethics committee representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials to establish the safety and efficacy of the product candidate for each proposed indication;
- preparation of and submission to the FDA of a biologics license application, or BLA, or a new drug application, or NDA, after completion of all pivotal clinical trials;
- potential review of the product application by an FDA advisory committee, where appropriate and if applicable;
- a determination by the FDA within 60 days of its receipt of a BLA or NDA to file the application for review;

- satisfactory completion of an FDA pre-approval inspection of the manufacturing facilities where the proposed product is produced to assess compliance with current Good Manufacturing Practices, or cGMP;
- potential FDA audit of the clinical trial sites that generated the data in support of the BLA or NDA; and
- FDA review and approval of a BLA or NDA prior to any commercial marketing or sale of the product in the United States.

The preclinical and clinical testing and approval process requires substantial time, effort, and financial resources, and we cannot be certain that any approvals for our product candidates will be granted on a timely basis, if at all.

An IND is a request for authorization from the FDA to administer an investigational new drug product to humans in clinical trials. The central focus of an IND submission is on the general investigational plan and the protocol(s) for human trials. The IND also includes results of animal and in vitro studies assessing the toxicology, pharmacokinetics, pharmacology, and pharmacodynamic characteristics of the product; chemistry, manufacturing, and controls information; and any available human data or literature to support the use of the investigational new drug. An IND must become effective before human clinical trials may begin. An IND will automatically become effective 30 days after receipt by the FDA, unless before that time the FDA raises concerns or questions related to the proposed clinical trials. In such a case, the IND may be placed on clinical hold and the IND sponsor and the FDA must resolve any outstanding concerns or questions before clinical trials can begin. Accordingly, submission of an IND may or may not result in the FDA allowing clinical trials to commence. The FDA may impose a clinical hold at any time during clinical trials and may impose a partial clinical hold that would limit trials, for example, to certain doses or for a certain length of time.

Clinical Trials

Clinical trials involve the administration of the investigational new drug to human subjects under the supervision of qualified investigators in accordance with Good Clinical Practices, or GCPs, which include the requirement that all research subjects provide their informed consent for their participation in any clinical trial. Clinical trials are conducted under protocols detailing, among other things, the objectives of the study, the parameters to be used in monitoring safety, and the efficacy 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. Additionally, approval must also be obtained from each clinical trial site's IRB before the trials may be initiated, and the IRB must monitor the trial until completed. There are also requirements governing the reporting of ongoing clinical trials and clinical trial results to public registries.

The clinical investigation of a drug is generally divided into three phases. Although the phases are usually conducted sequentially, they may overlap or be combined.

- *Phase 1.* The drug is initially introduced into healthy human subjects or patients with the target disease or condition. These studies are designed to evaluate the safety, dosage tolerance, metabolism and pharmacologic actions of the investigational new drug in humans, the side effects associated with increasing doses, and if possible, to gain early evidence on effectiveness.
- *Phase 2.* The drug is administered to a limited patient population to evaluate dosage tolerance and optimal dosage, identify possible adverse side effects and safety risks, and preliminarily evaluate efficacy.
- *Phase 3.* The drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites to generate enough data to evaluate dosage, clinical effectiveness and safety, to establish the overall benefit-risk relationship of the investigational new drug product, and to provide an adequate basis for physician labeling.

In some cases, the FDA may condition approval of a BLA or NDA for a product candidate on the sponsor's agreement to conduct additional clinical trials after approval. In other cases, a sponsor may voluntarily conduct additional clinical trials after approval to gain more information about the drug. Such post-approval studies are typically referred to as Phase 4 clinical trials.

Sponsors must also report to the FDA, within certain timeframes, serious and unexpected adverse reactions, any clinically important increase in the rate of a serious suspected adverse reaction over that listed in the protocol or investigator's brochure, or any findings from other studies or animal or in vitro testing that suggest a significant risk in humans exposed to the product candidate. The FDA, the IRB, or the clinical trial 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. Additionally, some clinical trials are overseen by an independent group of qualified experts organized by the clinical trial sponsor, known as a data safety monitoring board or committee. This group provides authorization for whether or not a trial may move forward at designated check points based on access to certain data from the trial. We may also suspend or terminate a clinical trial based on evolving business objectives or competitive climate.

The clinical trial process can take three to ten years or more to complete, and there can be no assurance that the data collected will support FDA approval or licensure of the product. Results from one trial are not necessarily predictive of results from later trials.

A drug being studied in clinical trials may be made available to individual patients in certain circumstances. Pursuant to the 21st Century Cures Act, or Cures Act, which was signed into law in December 2016, the manufacturer of an investigational drug for a serious disease or condition is required to make available, such as by posting on its website, its policy on evaluating and responding to requests for individual patient access to such investigational drug. This requirement applies on the later of 60 calendar days after the date of enactment of the Cures Act or the first initiation of a Phase 2 or Phase 3 trial of the investigational drug. *Submission of a BLA or NDA to the FDA.*

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, detailed investigational new drug product information is submitted to the FDA in the form of a BLA or NDA requesting approval to market the product for one or more indications. Under federal law, the submission of most BLAs and NDAs is subject to an application user fee. For fiscal year 2017, the application user fee is $2,038,100, and the sponsor of an approved BLA or NDA is also subject to annual product and establishment user fees, set at $97,750 per product and $512,200 per establishment. These fees are typically increased annually. Applications for orphan drug products are exempted from the BLA and NDA user fees and may be exempted from product and establishment user fees, unless the application includes an indication for other than a rare disease or condition.

A BLA or NDA for a new molecular entity must include all relevant data available from pertinent preclinical studies and clinical trials, including negative or ambiguous results as well as positive findings, together with detailed information relating to the product's chemistry, manufacturing, controls, and proposed labeling, among other things. Data can come from company-sponsored clinical trials intended to test the safety and effectiveness of a use of a product, or from a number of alternative sources, including trials initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and effectiveness of the investigational new drug product to the satisfaction of the FDA.

Once a BLA or NDA for a new molecular entity has been submitted, the FDA's goal is to review the application within ten months after it accepts the application for filing, or, if the application relates to an unmet medical need in a serious or life-threatening indication, six months after the FDA accepts the application for filing. The review process is often significantly extended by the FDA's requests for additional information or clarification.

Before approving a BLA or 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 a BLA or NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP.

The FDA is required to refer an application for a novel drug to an advisory committee or explain why such referral was not made. Typically, 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.

The FDA's Decision on a BLA or NDA

The FDA evaluates a BLA to determine whether the data demonstrate that the biologic is safe, pure, and potent, or effective, and an NDA to determine whether the drug is safe and effective. After the FDA evaluates the BLA or NDA and conducts inspections of manufacturing facilities where the product will be produced, it may issue an approval letter or a Complete Response Letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. A Complete Response Letter indicates that the review cycle of the application is complete and the application is not ready for approval. A Complete Response Letter may require additional clinical data or an additional pivotal Phase 3 clinical trial(s), or other significant, expensive and time-consuming requirements related to clinical trials, preclinical studies or manufacturing. Even if such additional information is submitted, the FDA may ultimately decide that the BLA or NDA does not satisfy the criteria for approval and issue a denial. The FDA could also approve the BLA or NDA with a Risk Evaluation and Mitigation Strategy, or REMS, plan to mitigate risks, which could include medication guides, physician communication plans, or elements to assure safe use, such as restricted distribution methods, patient registries and other risk minimization tools. The FDA also may condition approval on, among other things, changes to proposed labeling, development of adequate controls and specifications, or a commitment to conduct one or more post-market studies or clinical trials. Such post-market testing may include Phase 4 clinical trials and surveillance to further assess and monitor the product's safety and effectiveness after commercialization. Also, new government requirements, including those resulting from new legislation, may be established, or the FDA's policies may change, which could delay or prevent regulatory approval of our products under development.

Expedited Review and Accelerated Approval Programs

A sponsor may seek approval of its product candidate under programs designed to accelerate FDA's review and approval of BLAs and NDAs. For example, Fast Track Designation may be granted to a drug intended for treatment of a serious or life-threatening disease or condition that has potential to address unmet medical needs for the disease or condition. The key benefits of fast track designation are more frequent interactions with the FDA during development and testing, the eligibility for priority review, and rolling review, which is submission of portions of an application before the complete marketing application is submitted. Based on results of the Phase 3 clinical trial(s) submitted in a BLA or NDA, the FDA may grant the BLA or NDA a priority review designation, which sets the target date for FDA action on the application at six months after the FDA accepts the application for filing. Priority review is granted where there is evidence that the proposed product would be a significant improvement in the safety or effectiveness of the treatment, diagnosis, or prevention of a serious condition. If criteria are not met for priority review, the application is subject to the standard FDA review period of ten months after FDA accepts the application for filing. Priority review designation does not change the scientific/medical standard for approval or the quality of evidence necessary to support approval.

Under the accelerated approval program, the FDA may approve a BLA or NDA on the basis of either a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. Post-marketing trials or completion of ongoing trials after marketing approval are generally required to verify the drug's clinical benefit in relationship to the surrogate endpoint or ultimate outcome in relationship to the clinical benefit. In addition, the Food and Drug Administration Safety and Innovation Act, or FDASIA, which was enacted and signed into law in 2012, established the new Breakthrough Therapy designation. A sponsor may seek FDA designation of its product candidate as a breakthrough therapy if the drug is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. If so designated, the FDA shall act to expedite the development and review of the product's marketing application, including by meeting with the sponsor throughout the product's development, providing timely advice to the sponsor to ensure that the development program to gather preclinical and clinical data is as efficient as practicable, involving senior managers and experienced review staff in a cross-disciplinary review, and assigning a cross-disciplinary project lead for the FDA review team to facilitate an efficient review of the development program and to serve as a scientific liaison between the review team and the sponsor.

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.

Drug manufacturers are subject to periodic unannounced inspections by the FDA and state agencies for compliance with cGMP requirements. Changes to the manufacturing process are strictly regulated, and, depending on the significance of the change, may require prior FDA approval before being implemented. FDA regulations also require investigation and correction of any deviations from cGMP and impose reporting and documentation requirements upon us and any third-party manufacturers that we may decide to use. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain compliance with cGMP and other aspects of regulatory compliance.

We rely, and expect to continue to rely, on third parties for the production of clinical quantities of our product candidates, and expect to rely in the future on third parties for the production of commercial quantities. Future FDA and state inspections may identify compliance issues at our facilities or at the facilities of our contract manufacturers that may disrupt production or distribution, or require substantial resources to correct. In addition, discovery of previously unknown problems with a product or the failure to comply with applicable requirements may result in restrictions on a product, manufacturer or holder of an approved BLA or NDA, including withdrawal or recall of the product from the market or other voluntary, FDA-initiated or judicial action that could delay or prohibit further marketing. Also, new government requirements, including those resulting from new legislation, may be established, or the FDA's policies may change, which could delay or prevent regulatory approval of our products under development.

The FDA may withdraw 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 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 restrictions 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, untitled or warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending BLAs or NDAs or supplements to approved BLAs or NDAs, or suspension or revocation of licenses or withdrawal of 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.

Orphan Designation and Exclusivity

The FDA may grant orphan drug designation to drugs 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 making the drug for this type of disease or condition will be recovered from sales 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 is the first to receive FDA approval for the indication for which it has orphan designation, the product is entitled to orphan drug exclusivity, which means the FDA may not approve any other application to market the same drug 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.

Pediatric Trials and Exclusivity

Under the Pediatric Research Equity Act of 2003, or PREA, as amended, BLAs and NDAs must contain data to assess the safety and effectiveness of an investigational new drug product for the claimed indications in all relevant pediatric populations and to support dosing and administration for each pediatric subpopulation for which the drug is safe and effective. A sponsor who is planning to submit a marketing application for a drug product that includes a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration must submit an initial Pediatric Study Plan, or PSP, within sixty days of an end-of-phase 2 meeting or as may be agreed between the sponsor and the FDA. The initial PSP must include an outline of the pediatric study or studies that the sponsor plans to conduct, including study objectives and design, age groups, relevant endpoints and statistical approach, or a justification for not including such detailed information, and any request for a deferral of pediatric assessments or a full or partial waiver of the requirement to provide data from pediatric studies along with supporting information. 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 if certain criteria are met. The FDA and the sponsor must reach agreement on the PSP. A sponsor can submit amendments to an agreed-upon initial PSP at any time if changes to the pediatric plan need to be considered based on data collected from preclinical studies, early phase clinical trials, and/or other clinical development programs. The requirements for pediatric data do not apply to any drug for an indication for which orphan designation has been granted.

Pediatric exclusivity is another type of non-patent exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including the five-year and three-year non-patent and orphan exclusivity. This six-month exclusivity may be granted if a BLA or NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of FDA-requested pediatric trials are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection covering the product are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot accept or approve another application relying on the BLA or NDA sponsor's data.

Patent Term Restoration

Depending upon the timing, duration, and specifics of the FDA approval of the use of our product candidates, some of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Amendments. The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14 years from the product's approval date. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of a BLA or NDA, plus the time between the submission date and the approval of that application, except that the review period is reduced by any time during which the applicant failed to exercise due diligence. Only one patent applicable to an approved product is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent and within 60 days of the product's approval. The U.S. Patent and Trademark Office, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. In the future, we may apply for restoration of patent term for one of our currently owned or licensed patents to add patent life beyond its current expiration date, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant BLA or NDA.

Biosimilars and Exclusivity

The Patient Protection and Affordable Care Act, or Affordable Care Act, signed into law on March 23, 2010, includes a subtitle called the Biologics Price Competition and Innovation Act of 2009, or BPCI Act, which created an abbreviated approval pathway for biological products shown to be biosimilar to, or interchangeable with, an FDA-licensed reference biological product. This amendment to the PHSA attempts to minimize duplicative testing. Biosimilarity, which requires that there be no clinically meaningful differences between the biological product and the reference product in terms of safety, purity, and potency, can be shown through analytical studies, animal studies, and a clinical trial or trials. Interchangeability requires that a product is biosimilar to the reference product and the product must demonstrate that it can be expected to produce the same clinical results as the reference product and, for products administered multiple times, the biologic and the reference biologic may be switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biologic.

A reference biologic is granted twelve years of exclusivity from the time of first licensure of the reference product. The first biologic product submitted under the abbreviated approval pathway that is determined to be interchangeable with the reference product has exclusivity against other biologics submitting under the abbreviated approval pathway for the lesser of (i) one year after the first commercial marketing, (ii) eighteen months after approval if there is no legal challenge, (iii) eighteen months after the resolution in the applicant's favor of a lawsuit challenging the biologics' patents if an application has been submitted, or (iv) 42 months after the application has been approved if a lawsuit is ongoing within the 42-month period.

Abbreviated New Drug Applications for Generic Drugs

In 1984, with passage of the Hatch-Waxman Amendments, Congress authorized the FDA to approve generic drugs that are the same as drugs previously approved by the FDA under the NDA provisions of the statute. To obtain approval of a generic drug, an applicant must submit an abbreviated new drug application, or ANDA, to the agency. In support of such applications, a generic manufacturer may rely on the preclinical and clinical testing previously conducted for a drug product previously approved under an NDA, known as the reference listed drug, or RLD.

Specifically, in order for an ANDA to be approved, the FDA must find that the generic version is identical to the RLD with respect to the active ingredients, the route of administration, the dosage form, and the strength of the drug. At the same time, the FDA must also determine that the generic drug is "bioequivalent" to the innovator drug. Under the statute, a generic drug is bioequivalent to an RLD if "the rate and extent of absorption of the generic drug do not show a significant difference from the rate and extent of absorption of the listed drug. . . ."

Upon approval of an ANDA, the FDA indicates that the generic product is "therapeutically equivalent" to the RLD and it assigns a therapeutic equivalence rating to the approved generic drug in its publication "Approved Drug Products with Therapeutic Equivalence Evaluations," also referred to as the "Orange Book." Physicians and pharmacists consider an "AB" therapeutic equivalence rating to mean that a generic drug is fully substitutable for the RLD. In addition, by operation of certain state laws and numerous health insurance programs, the FDA's designation of an "AB" rating often results in substitution of the generic drug without the knowledge or consent of either the prescribing physician or patient.

The FDCA provides a period of five years of non-patent exclusivity for a new drug containing a new chemical entity. In cases where such exclusivity has been granted, an ANDA may not be filed with the FDA until the expiration of five years unless the submission is accompanied by a Paragraph IV certification, in which case the applicant may submit its application four years following the original product approval. The FDCA also provides for a period of three years of exclusivity if the NDA includes reports of one or more new clinical investigations, other than bioavailability or bioequivalence studies, that were conducted by or for the applicant and are essential to the approval of the application. This three-year exclusivity period often protects changes to a previously approved drug product, such as a new dosage form, route of administration, combination or indication.

Hatch-Waxman Patent Certification and the 30-Month Stay

Upon approval of an NDA or a supplement thereto, NDA sponsors are required to list with the FDA each patent with claims that cover the applicant's product or a method of using the product. Each of the patents listed by the NDA sponsor is published in the Orange Book. When an ANDA applicant files its application with the FDA, the applicant is required to certify to the FDA concerning any patents listed for the reference product in the Orange Book, except for patents covering methods of use for which the ANDA applicant is not seeking approval.

Specifically, the applicant must certify with respect to each patent that:

- the required patent information has not been filed;
- the listed patent has expired;
- the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or
- the listed patent is invalid, unenforceable or will not be infringed by the new product.

A certification that the new product will not infringe the already approved product's listed patents or that such patents are invalid or unenforceable is called a Paragraph IV certification. If the applicant does not challenge the listed patents or indicates that it is not seeking approval of a patented method of use, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired.

If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days after the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months after the receipt of the Paragraph IV notice, expiration of the patent, or a decision in the infringement case that is favorable to the ANDA applicant.

European Union/Rest of World Government Regulation

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 trials and any commercial sales and distribution of our products. The cost of establishing a regulatory compliance system for numerous varying jurisdictions can be very significant. Although many of the issues discussed above with respect to the United States apply similarly in the context of the European Union and in other jurisdictions, the approval process varies between countries and jurisdictions and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries and jurisdictions might differ from and be longer than that required to obtain FDA approval. Regulatory approval in one country or jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country or jurisdiction may negatively impact the regulatory process in others.

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 trials 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 trial application much like the IND prior to the commencement of human clinical trials. In the European Union, for example, a clinical trial authorization application, or CTA, must be submitted for each clinical protocol to each country's national health authority and an independent ethics committee, much like the FDA and IRB, respectively. Once the CTA is accepted in accordance with a country's requirements, the clinical trial may proceed.

The requirements and process governing the conduct of clinical trials vary from country to country. In all cases, the clinical trials are conducted in accordance with good clinical practices, or GCP, the applicable regulatory requirements, and the ethical principles that have their origin in the Declaration of Helsinki.

To obtain regulatory approval of an investigational medicinal product under European Union regulatory systems, we must submit a marketing authorization application. The content of the BLA or NDA filed in the United States is similar to that required in the European Union, with the exception of, among other things, country-specific document requirements.

For other countries outside of the European Union, such as countries in Eastern Europe, Latin America or Asia, the requirements governing product licensing, pricing, and reimbursement vary from country to country.

Countries that are part of the European Union, as well as countries outside of the European Union, have their own governing bodies, requirements, and processes with respect to the approval of pharmaceutical and biologic products. 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.

Authorization Procedures in the European Union

Medicines can be authorized in the European Union by using either the centralized authorization procedure or national authorization procedures.

- *Centralized procedure*. The EMA implemented the centralized procedure for the approval of human medicines to facilitate marketing authorizations that are valid throughout the European Economic Area, or EEA, which is comprised of the 28 member states of the European Union plus Norway, Iceland, and Lichtenstein. This procedure results in a single marketing authorization issued by the EMA that is valid across the EEA. The centralized procedure is compulsory for human medicines that are: derived from biotechnology processes, such as genetic engineering, contain a new active substance indicated for the treatment of certain diseases, such as HIV/AIDS, cancer, diabetes, neurodegenerative disorders or autoimmune diseases and other immune dysfunctions, and officially designated orphan medicines.
- For medicines that do not fall within these categories, an applicant has the option of submitting an application for a centralized marketing authorization to the European Commission following a favorable opinion by the EMA, as long as the medicine concerned is a significant therapeutic, scientific or technical innovation, or if its authorization would be in the interest of public health.
- *National authorization procedures*. There are also two other possible routes to authorize medicinal products in several European Union countries, which are available for investigational medicinal products that fall outside the scope of the centralized procedure:
- *Decentralized procedure*. Using the decentralized procedure, an applicant may apply for simultaneous authorization in more than one European Union country of medicinal products that have not yet been authorized in any European Union country and that do not fall within the mandatory scope of the centralized procedure.
- *Mutual recognition procedure*. In the mutual recognition procedure, a medicine is first authorized in one European Union Member State, in accordance with the national procedures of that country. Following this, further marketing authorizations can be sought from other European Union countries in a procedure whereby the countries concerned agree to recognize the validity of the original, national marketing authorization.

In some cases, a Pediatric Investigation Plan, or PIP, or a request for waiver or deferral, is required for submission prior to submitting a marketing authorization application. A PIP describes, among other things, proposed pediatric trials and their timing relative to clinical trials in adults.

New Chemical Entity Exclusivity

In the European Union, new chemical entities, sometimes referred to as new active substances, qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity. This data exclusivity, if granted, prevents regulatory authorities in the European Union from referencing the innovator's data to assess a generic (abbreviated) application for eight years, after which a generic application can be submitted, and the innovator's data may be referenced, but not approved for two years. The overall ten-year period will be extended to a maximum of eleven years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies.

Orphan Designation and Exclusivity

In the European Union, the European Commission, after reviewing the opinion of the EMA's Committee for Orphan Medicinal Products, or COMP, grants orphan drug designation to promote the development of products that are intended for the diagnosis, prevention or treatment of life-threatening or chronically debilitating conditions that affect not more than 5 in 10,000 persons in the European Union Community, or when, without incentives, it is unlikely that sales of such products in the European Union would be sufficient to justify the necessary investment in developing the products. Additionally, orphan drug designation is only available where no satisfactory method of diagnosis, prevention, or treatment of the condition has been authorized (or the product would be a significant benefit to those affected).

In the European Union, orphan drug designation entitles a party to financial incentives such as reduction of fees or fee waivers and ten years of market exclusivity is granted following medicinal product approval. This period may be reduced to six years if the orphan drug designation criteria are no longer met, including where it is shown that the product is sufficiently profitable not to justify maintenance of market exclusivity. Market exclusivity would not prevent the approval of a similar drug that is shown to be safer, more effective or otherwise clinically superior.

Orphan drug designation must be requested before submitting an application for marketing approval. Orphan drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process.

Exceptional Circumstances/Conditional Approval

Orphan drugs or drugs with unmet medical needs may be eligible for European Union approval under exceptional circumstances or with conditional approval. Approval under exceptional circumstances may be applicable to orphan products and is used when an applicant is unable to provide comprehensive data on the efficacy and safety under normal conditions of use because the indication for which the product is intended is encountered so rarely that the applicant cannot reasonably be expected to provide comprehensive evidence, when the present state of scientific knowledge does not allow comprehensive information to be provided, or when it is medically unethical to collect such information. Conditional marketing authorization may be applicable to orphan medicinal products, medicinal products for seriously debilitating or life-threatening diseases, or medicinal products to be used in emergency situations in response to recognized public threats. Conditional marketing authorization can be granted on the basis of less complete data than is normally required in order to meet unmet medical needs and in the interest of public health, provided the risk-benefit balance is positive, it is likely that the applicant will be able to provide the comprehensive clinical data, and unmet medical needs will be fulfilled. Conditional marketing authorization is subject to certain specific obligations to be reviewed annually.

Accelerated Review

Under the centralized procedure in the European Union, the maximum timeframe for the evaluation of a marketing authorization application is 210 days (excluding clock stops, when additional written or oral information is to be provided by the applicant in response to questions asked by the EMA's Committee for Medicinal Products for Human Use, or CHMP). Accelerated evaluation might be granted by the CHMP in exceptional cases, when a medicinal product is expected to be of a major public health interest, particularly from the point of view of therapeutic innovation. In this circumstance, EMA ensures that the opinion of the CHMP is given within 150 days, excluding clock stops.

Pharmaceutical Coverage, Pricing and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any products for which we obtain regulatory approval. In the United States and in other countries, sales of any products for which we receive regulatory approval for commercial sale will depend in part on the availability of coverage and reimbursement from third-party payors. Third-party payors include government authorities, managed care providers, private health insurers and other organizations. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the reimbursement rate that the payor will pay for the product. Third-party payors may limit coverage to specific products on an approved list, or formulary, which might not include all of the FDA-approved products for a particular indication. Moreover, a payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Adequate third- party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

Third-party payors are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. In order to obtain coverage and reimbursement for any product that might be approved for sale, we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain regulatory approvals. Our product candidates may not be considered medically necessary or cost-effective. If third-party payors do not consider a product to be cost-effective compared to other available therapies, they may not cover the product after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow a company to sell its products at a profit.

The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost containment programs to limit the growth of government-paid health care costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. By way of example, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, collectively, the Affordable Care Act, contains provisions that may reduce the profitability of drug products, including, for example, increased rebates for drugs sold to Medicaid programs, extension of Medicaid rebates to Medicaid managed care plans, mandatory discounts for certain Medicare Part D beneficiaries and annual fees based on pharmaceutical companies' share of sales to federal health care programs. Some of the provisions of the Affordable Care Act 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, any law replacing elements of it, or the political uncertainty surrounding its repeal or replacement on our business remains unclear. Adoption of government controls and measures, and tightening of restrictive policies in jurisdictions with existing controls and measures, could limit payments for pharmaceuticals.

In the European Community, governments influence the price of pharmaceutical products through their pricing and reimbursement rules and control of national health care systems that fund a large part of the cost of those products to consumers. Some jurisdictions operate positive and negative list systems under which products may only be marketed once a reimbursement price has been agreed to by the government. To obtain reimbursement or pricing approval, some of these countries may require the completion of clinical trials that compare the cost-effectiveness of a particular product candidate to currently available therapies. Other member states allow companies to fix their own prices for medicines, but monitor and control company profits. The downward pressure on health care costs in general, particularly prescription drugs, has become very intense. As a result, increasingly high barriers are being erected to the entry of new products. In addition, in some countries, cross-border imports from low-priced markets exert a commercial pressure on pricing within a country.

The marketability of any products for which we receive regulatory approval for commercial sale may suffer if the government and third-party payors fail to provide adequate coverage and reimbursement. In addition, an increasing emphasis on cost containment measures in the United States and other countries has increased and we expect will continue to increase the pressure on pharmaceutical pricing. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

Other Healthcare Laws and Compliance Requirements

If we obtain regulatory approval for any of our product candidates, we may be subject to various federal and state laws targeting fraud and abuse in the healthcare industry. These laws may impact, among other things, our proposed sales, marketing and education programs. In addition, we may be subject to patient privacy regulation by both the federal government and the states in which we conduct our business. The laws that may affect our ability to operate include:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, to induce, or in return for, the purchase or recommendation of an item or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs;
- federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payors that are false or fraudulent;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created new federal criminal statutes that prohibit executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters;
- the federal transparency laws, including the provision of the Affordable Care Act referred to as the federal Physician Payment Sunshine Act, that requires drug and biologics manufacturers to disclose payments and other transfers of value provided to physicians and teaching hospitals and ownership interests of physicians and their immediate family members;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and its implementing regulations, which imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information; and
- state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws that may apply to items or services reimbursed by any third-party payor, including commercial insurers, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

The Affordable Care Act broadened the reach of the fraud and abuse laws by, among other things, amending the intent requirement of the federal Anti-Kickback Statute and the applicable criminal healthcare fraud statutes contained within 42 U.S.C. § 1320a-7b. Pursuant to the statutory amendment, a person or entity no longer needs to have actual knowledge of this statute or specific intent to violate it in order to have committed a violation. In addition, the Affordable Care Act provides 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 civil False Claims Act or the civil monetary penalties statute. Many states have adopted laws similar to the federal Anti-Kickback Statute, some of which apply to the referral of patients for healthcare items or services reimbursed by any source, not only the Medicare and Medicaid programs.

We are also subject to the U.S. Foreign Corrupt Practices Act, or FCPA, which prohibits improper payments or offers of payments to foreign governments and their officials for the purpose of obtaining or retaining business. Safeguards we implement to discourage improper payments or offers of payments by our employees, consultants, and others may be ineffective, and violations of the FCPA and similar laws may result in severe criminal or civil sanctions, or other liabilities or proceedings against us, any of which would likely harm our reputation, business, financial condition and result of operations.

If 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, exclusion from participation in government healthcare programs, such as Medicare and Medicaid and imprisonment, damages, fines and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Employees

As of March 9, 2017 we had 58 full-time employees. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

Financial Information about Segments

We operate in a single accounting segment. Refer to Note 1, "Organization, Business and Basis of Presentation" in the Notes to Consolidated Financial Statements included elsewhere in this report.

Emerging Growth Company

We completed our initial public offering, or IPO, in May 2015, in which we sold 6,164,000 shares of common stock, at a public offering price of $14.00 per share, the net proceeds of which totaled $75.9 million, after deducting underwriting discounts and commissions and offering expenses incurred by us. We qualify as an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, as amended, or the JOBS Act. As an emerging growth company, we may take advantage of specified reduced disclosure and other requirements that are otherwise applicable generally to public companies. We would cease to be an emerging growth company on the date that is the earliest of: (i) the last day of the fiscal year in which we have total annual gross revenues of $1 billion or more; (ii) December 31, 2020; (iii) the date on which we have issued more than $1 billion in nonconvertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the SEC.

Corporate Information

We were incorporated under the laws of the State of Delaware in September 2005. Our principal executive office is located at 3545 John Hopkins Court, Suite #250, San Diego, California 92121, and our telephone number is (858) 731-8389. Our website address is www.atyrpharma.com. We do not incorporate the information on or accessible through our website into this Annual Report, and you should not consider any information on, or that can be accessed through, our website as part of this Annual Report.

You are advised to read this Annual Report in conjunction with other reports and documents that we file from time to time with the SEC. In particular, please read our final prospectus filed with the SEC on May 7, 2015 under Rule 424(b) of the Securities Act of 1933, as amended, our Quarterly Reports on Form 10-Q and any Current Reports on Form 8-K that we may file from time to time. You may obtain copies of these reports directly from us or from the SEC at the SEC's Public Reference Room at 100 F Street, N.E. Washington, D.C. 20549. In addition, the SEC maintains information for electronic filers (including aTyr Pharma, Inc.) at its website at www.sec.gov. The public may obtain information regarding the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. We make our periodic and current reports available on our internet website, free of charge, as soon as reasonably practicable after such material is electronically filed with, or furnished to, the SEC.

Item 1A. Risk Factors

You should carefully consider the following risk factors, as well as the other information in this Annual Report on Form 10-K, and in our other public filings. The occurrence of any of these risks could harm our business, financial condition, results of operations and/or growth prospects or cause our actual results to differ materially from those contained in forward-looking statements we have made in this report and those we may make from time to time. You should consider all of the risk factors described in our public filings when evaluating our business.

Risks related to the discovery, development and regulation of our Physiocrine-based product candidates

Resolaris, Stalaris and any other product candidates that we may develop from our discovery engine represent novel therapeutic approaches, which may cause significant delays or may not result in any commercially viable drugs.

We have concentrated our research and development efforts on Physiocrine biology, a new area of biology, and our future success is highly dependent on the successful development of Physiocrine-based product candidates, including Resolaris, Stalaris and additional product candidates arising from the Resokine pathway or other pathways. Physiocrine-based biology represents a novel approach to drug discovery and development, and to our knowledge, no drugs have been developed using, or based upon, this approach. Despite the successful development of other naturally occurring proteins, such as erythropoietin and insulin, as therapeutics, Physiocrines represent a novel class of protein therapeutics, and our development of these therapeutics is based on our new understanding of human physiology. In particular, the mechanism of action of Physiocrines and their role in immuno-modulation and tissue regeneration have not been studied extensively, nor has the safety of this class of protein therapeutics been evaluated extensively in humans. The Physiocrines that we elect to develop may not have the physiological functions that we currently ascribe to them, may have limited or no therapeutic applications, or may present safety problems of which we are not yet aware. We cannot be sure that our discovery engine will yield Physiocrine-based therapeutic product candidates that are safe, effective, approvable by regulatory authorities, manufacturable, scalable, or profitable.

Because our work in Physiocrine biology and our product candidates represent a new therapeutic approach, developing and commercializing our product candidates subjects us to a number of challenges, including:

- defining indications within our targeted rare diseases and clinical endpoints within each indication that are appropriate to support regulatory approval;
- obtaining regulatory approval from the U.S. Food and Drug Administration, or the FDA, and other regulatory authorities that have little or no experience with the development of Physiocrine-based therapeutics;
- educating medical personnel regarding the potential side effect profile of each of our product candidates, such as the potential for the development of antibodies against our purified protein therapeutics;
- developing processes for the safe administration of these product candidates, including long-term follow-up for all patients who receive our product candidates;
- sourcing clinical and, if approved, commercial supplies for the materials used to manufacture and process our product candidates;
- developing a manufacturing process and distribution network that ensures consistent manufacture of our product candidates in compliance with current Good Manufacturing Practices, or cGMPs, and related requirements, with a cost of goods that allows for an attractive return on investment;
- establishing sales and marketing capabilities after obtaining any regulatory approval to gain market acceptance; and
- developing therapeutics for rare and more common diseases or indications beyond those addressed by our current product candidates.

Moreover, public perception of safety issues, including adoption of new therapeutics or novel approaches to treatment, may adversely influence the willingness of subjects to participate in clinical trials, or if approved, of physicians to adopt and prescribe novel therapeutics. Physicians, hospitals and third-party payors often are slow to adopt new products, technologies and treatment practices. Physicians may decide the therapy is too complex or unproven to adopt and may choose not to administer the therapy. Based on these and other factors, healthcare providers and payors may decide that the benefits of any Physiocrine-based therapeutic for which we receive regulatory approval do not or will not outweigh its costs. Any inability to successfully develop commercially viable drugs would have an adverse impact on our business, prospects, financial condition and results of operations.

If we are unable to successfully complete or otherwise advance clinical development, obtain regulatory or marketing approval for, or successfully commercialize, Resolaris or Stalaris, or experience significant delays in doing so, our business will be materially harmed.

To date, we have expended significant time, resources and effort on the discovery and development of Resolaris, including conducting preclinical studies and our clinical trials. We have not yet commenced or completed any evaluation of Resolaris in human clinical trials designed to demonstrate efficacy to the satisfaction of the FDA. We have not yet commenced clinical development of Stalaris. We currently generate no revenue from the sale of any product, and our ability to generate product revenues and to achieve commercial success, which we do not expect will occur for many years, if ever, will initially depend on our ability to successfully develop, obtain regulatory approval for and commercialize Resolaris or Stalaris for the treatment of one or more of our target rare disease indications in the United States and any foreign jurisdictions. Before we can market or sell Resolaris or Stalaris in the United States or foreign jurisdictions, we will need to commence and complete additional clinical trials (including larger, pivotal trials, which we have not yet commenced), manage clinical and manufacturing activities, obtain necessary regulatory approvals from the FDA in the United States and from similar regulatory authorities in other jurisdictions, obtain adequate clinical and commercial manufacturing supplies, build commercial capabilities, which may include entering into a marketing collaboration with a third party, and in some jurisdictions, obtain reimbursement authorization, among other things. We cannot assure you that we will be able to successfully complete the necessary clinical trials, obtain regulatory approvals, secure an adequate commercial supply for, or otherwise successfully commercialize, Resolaris or Stalaris. If we do not receive regulatory approvals for Resolaris or Stalaris, and even if we do obtain regulatory approvals, we may never generate significant revenues, if any, from commercial sales. If we fail to successfully commercialize Resolaris or Stalaris, we may be unable to generate sufficient revenues to sustain and grow our company, and our business, prospects, financial condition and results of operations will be adversely affected.

Data generated in our preclinical studies and patient sample data relating to the Resokine pathway may not be predictive or indicative of the immuno-modulatory activity or therapeutic effects, if any, of Resolaris in patients.

Our scientists discovered the Resokine pathway using *in vivo* screening systems designed to test potential immuno-modulatory activity in animal models of severe immune activity or inflammation, combined with data relating to the potential blockade of the Resokine pathway in a population of patients with myopathy that occurs in a particular rare disease, anti-synthetase syndrome, with Jo-1 antibodies. Translational medicine, or the application of basic scientific findings to develop therapeutics that promote human health, is subject to a number of inherent risks. In particular, scientific hypotheses formed from nonclinical observations may prove to be incorrect, and the data generated in animal models or observed in limited patient populations may be of limited value, and may not be applicable in clinical trials conducted under the controlled conditions required by applicable regulatory requirements and our protocols. For example, we have not extensively studied the activity of the Resokine pathway in patients with rare genetic myopathies with an immune component, or RMICs, which forms the basis for our clinical trials of Resolaris in FSHD and limb-girdle muscular dystrophy 2B, or LGMD2B, nor have we evaluated the activity of the Resokine pathway in patients with interstitial lung disease, or ILD. Our knowledge of the activity of this pathway in Jo-1 antibody patients may not be applicable to our target patient populations in RMICs or rare pulmonary diseases with an immune component, or RPICs. In addition, our classification of diseases based on the existence of immune cell invasion (RMICs and RPICs) and our hypothesis that these represent potential indications for Resolaris and Stalaris may not prove to be therapeutically relevant. Accordingly, the conclusions that we have drawn from animal studies and patient sample data regarding the potential immuno-modulatory activity of molecules containing the immuno-modulatory domain, or iMod domain, may not be substantiated in other animal models or in clinical trials. Any failure to demonstrate in controlled clinical trials the requisite safety and efficacy of Resolaris, Stalaris or other product candidates that we may develop will adversely affect our business, prospects, financial condition and results of operations.

We have not studied Resolaris, Stalaris or any of our other product candidates in any human clinical trials designed primarily to show efficacy.

Preclinical and clinical data are often susceptible to varying interpretations and analyses, which may delay, limit or prevent regulatory approval. Many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products. Accordingly, our earlier preclinical and clinical studies should not be relied upon as evidence that our current or future clinical trials will succeed. Study designs and results from previous studies are not necessarily predictive of our future clinical trial designs or results, and initial results may not be confirmed upon full analysis of the complete study data. In particular, Resolaris may not achieve positive results in our current and planned clinical trials in RMICs, and any results observed in our Phase 1b/2 clinical trials of Resolaris in patients with FSHD and LGMD2B may not be predictive of results for any future clinical studies. Stalaris may not achieve positive results in our planned clinical trials in healthy subjects and in RPICs or any other clinical studies. In addition, study data from our clinical trials in adult patients might not be predictive of safety, tolerability, immunogenicity or activity in young adults and children. Additionally, Resolaris and Stalaris may fail to show the desired safety and efficacy in later stages of clinical development, such as pivotal clinical trials, despite having successfully advanced through initial clinical trials. Any failure of Resolaris, Stalaris or any other product candidates that we may develop at any stage in the clinical development process would have a material adverse impact on our business, prospects, financial condition and results of operations.

Because we are developing novel product candidates for the treatment of diseases in which there is little clinical drug development experience and, in some cases, are using new endpoints or methodologies, the regulatory pathways for approval are not well defined, and as a result, there is greater risk that our clinical trials will not result in our desired outcomes.

Our initial clinical focus is on the development of Physiocrine-based therapeutics for the treatment of rare diseases, including FSHD, LGMD2B and potentially DMD, where patients may benefit from the activation of immuno-modulatory pathways. There are currently no approved treatments for FSHD or LGMD2B. As a result, the design and conduct of clinical trials for these indications are subject to increased risk, and we may experience setbacks with our ongoing or planned clinical trials for Resolaris or other product candidates that we may develop because of the limited clinical experience in our target indications. In particular, regulatory authorities in the United States and European Union have not issued definitive guidance as to how to measure and achieve efficacy. In later stage trials, we may not achieve a pre-specified endpoint with statistical significance in our planned clinical trials of Resolaris in this indication or in other indications where there is limited or no regulatory guidance regarding appropriate clinical endpoints, which would decrease the chance of obtaining marketing approval for Resolaris. Additionally, it is difficult to establish clinically relevant endpoints for some of these indications because it may take a long time before any therapeutic effects of a drug can be observed.

We could also face challenges in designing clinical trials and obtaining regulatory approval for product candidates from our discovery engine due to the lack of historical clinical trial experience for this novel class of therapeutics. At the moment, because no Physiocrine-based products have received regulatory approval anywhere in the world, it is difficult to determine whether regulatory agencies will be receptive to the approval of our product candidates and to predict the time and cost associated with obtaining regulatory approval. The clinical trial requirements of the FDA and other regulatory agencies and the criteria these regulators use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty and intended use and market of the potential products. The regulatory approval process for novel product candidates such as ours can be more expensive and take longer than for other, better known or more extensively studied classes of product candidates. Any inability to design clinical trials with protocols and endpoints acceptable to applicable regulatory authorities, and to obtain regulatory approvals for our product candidates, would have an adverse impact on our business, prospects, financial condition and results of operations.

We may encounter substantial delays and other challenges in our clinical trials or we may fail to demonstrate safety and efficacy to the satisfaction of applicable regulatory authorities.

Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must conduct extensive clinical trials to demonstrate the safety and efficacy of the product candidates in humans. Clinical trials are expensive, time-consuming, often delayed and uncertain as to outcome. We cannot guarantee that our ongoing and planned clinical trials of Resolaris in RMICs, planned clinical trials of Stalaris in RPICs, or any other clinical trials that we may plan to conduct, will be initiated or conducted as planned or completed on schedule, if at all. Following our submission of an investigational new drug application, or IND, to the FDA to evaluate Resolaris in our Phase 1b/2 trial in adult patients with FSHD in the United States, our IND was placed on full clinical hold to address the nonclinical issue of the comparability of the drug substance used in our preclinical toxicology studies to that used in our Phase 1 clinical trial and proposed for use in the U.S. clinical trial in FSHD patients. We responded to the FDA's comparability request, and, in January 2015, our IND was removed from full clinical hold, allowing us to initiate the Phase 1b/2 trial in the United States. Our IND was placed on partial clinical hold, which prohibited the evaluation of Resolaris at doses higher than 3.0 mg/kg. The partial clinical hold was lifted in December 2016. We cannot assure you that our product candidates will not be subject to new clinical holds or significant delay in the future. Any inability to initiate or complete our clinical trials of Resolaris, Stalaris or other product candidates in the United States, as a result of clinical holds or otherwise, would delay our clinical development plans, may require us to incur additional clinical development costs and could impair our ability to obtain U.S. regulatory approval for such product candidates.

A failure of one or more clinical trials can occur at any stage of testing, and our clinical trials may not be successful. Events that may prevent successful or timely completion of clinical development include, but are not limited to:

- inability to generate sufficient preclinical, toxicology, or other in vivo or in vitro data to support the initiation of human clinical trials, including trials of certain dosages;
- delays in reaching consensus with regulatory agencies on trial design;
- delays in reaching agreement on acceptable terms with prospective clinical contract research organizations, or CROs, and clinical trial sites;
- delays in obtaining required Institutional Review Board, or IRB, or Ethics Committee approval at each clinical trial site;
- delays in recruiting suitable patients to participate in our clinical trials, or delays that may result if the number of patients required for a clinical trial is larger than we anticipate;
- imposition of a clinical hold by regulatory agencies, which may occur after our submission of data to these agencies or an inspection of our clinical trial operations or trial sites;

- failure by our CROs, investigators, other third parties or us to adhere to clinical trial requirements;
- failure to perform in accordance with the FDA's good clinical practices, or GCPs, or applicable regulatory requirements in other countries;
- delays in the testing, validation, manufacturing and delivery of our product candidates to the clinical sites;
- delays in having patients complete participation in a trial or return for post-treatment follow-up;
- disagreements with regulators regarding our interpretation of data from preclinical studies or clinical trials;
- occurrence of adverse events associated with the product candidate that are viewed to outweigh its potential benefits; or
- changes in regulatory requirements and guidance that require amending or submitting new clinical protocols.

Any delay in or inability to successfully complete preclinical and clinical development could result in additional costs to us and impair our ability to generate revenue. In addition, if we make manufacturing or formulation changes to our product candidates (including recent changes in our contract manufacturer, production capacity and manufacturing cell line), we may need to conduct additional studies to bridge our modified product candidates to earlier versions. Clinical trial delays could also shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do, which could impair our ability to obtain orphan exclusivity and successfully commercialize our product candidates and may harm our business and results of operations.

If the results of our clinical trials are perceived to be negative or inconclusive, or if there are safety concerns or adverse events associated with our product candidates, we may:

- be required to perform additional clinical trials to support approval or be subject to additional post-marketing testing requirements;
- be delayed in obtaining marketing approval for our product candidates, if at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings;
- be subject to changes in the way the product is manufactured or administered;
- have regulatory authorities withdraw their approval of the product or impose restrictions on its distribution in the form of a modified risk evaluation and mitigation strategy, or REMS;
- be subject to litigation; or
- experience damage to our reputation.

To date, the safety and efficacy of Physiocrine-based therapeutics in humans has not been studied to any significant extent. Accordingly, our product candidates could potentially cause adverse events that have not yet been predicted. In addition, the inclusion of critically ill patients in our clinical trials may result in deaths or other adverse medical events due to the natural progression of the disease. As described above, any of these events could prevent us from successfully completing the clinical development of our product candidates and impair our ability to commercialize any products.

Resolaris, Stalaris and any other product candidates that we may discover and develop may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial profile of an approved label, or result in significant negative consequences following marketing approval, if any.

Undesirable side effects caused by Resolaris, Stalaris and any other product candidates that we may discover or develop, or safety, tolerability or toxicity issues that may occur in our preclinical studies, clinical trials or in the future, could cause us or regulatory authorities to interrupt, restrict, 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.

In our Phase 1b/2 clinical trials, we have observed low levels of antibodies to Resolaris in some subjects in response to the administration of Resolaris. Although such elevated antibody observations were without associated clinical symptoms, the development of higher levels of such antibodies over a longer course of treatment may ultimately limit the efficacy of Resolaris and trigger a negative autoimmune response, including the development of anti-synthetase syndrome. Anti-synthetase syndrome can include one or more of the following clinical features: ILD, inflammatory myopathy and inflammatory polyarthritis. Other symptoms which may occur in this setting include fever, weight loss, fatigue, Raynaud's phenomenon of the digits, rash and difficulty swallowing. Some patients in our Phase 1b/2 clinical trials have experienced generalized infusion related reactions, or IRRs, and discontinued dosing. We established procedural measures, including a decreased concentration and intravenous delivery rate of Resolaris, in an effort to minimize the occurrence of generalized IRRs and the formation of anti-drug antibodies. After implementation of these procedures, we did observe a decreased rate of IRRs in our clinical trials, but we cannot assure that these measures will continue to be effective in minimizing the occurrence of generalized IRRs or the formation of anti-drug antibodies, or result in the retention of patients in our trials. Generalized IRRs and other complications or side effects could harm further development and/or commercialization of Resolaris, Stalaris and any other product candidates. Additionally, our product candidates are designed to be administered by intravenous injection, which may cause side effects, including acute immune responses and injection site reactions. The risk of adverse immune responses remains a significant concern for protein therapeutics, and we cannot assure that these or other risks will not occur in any of our clinical trials for Resolaris, Stalaris or other product candidates we may develop. There is also a risk of delayed adverse events as a result of long-term exposure to protein therapeutics that must be administered repeatedly for the management of chronic conditions, such as the development of antibodies, which may occur over time. If any such adverse events occur, which may include the development of anti-synthetase syndrome from antibodies or the occurrence of IRRs associated with antibodies, further advancement of our clinical trials could be halted or delayed, which would have a material adverse effect on our business, prospects, financial condition and results of operations.

If one or more of our product candidates receives marketing approval, and we or others later identify undesirable side effects or other safety concerns caused by such products, a number of potentially significant negative consequences could result, including but not limited to:

- regulatory authorities may withdraw approvals or suspend licenses of such products;
- regulatory authorities may require additional warnings on the label;
- we may be required to create a REMS plan, which could include a medication guide outlining the risks of such side effects for distribution to patients, a communication plan for healthcare providers, or other elements to assure safe use;
- 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 product candidate, if approved, and could significantly harm our business, prospects, financial condition and results of operations.

We may not be successful in our efforts to identify or discover additional product candidates.

A key element of our strategy is to leverage our discovery engine to identify tRNA synthetases that exhibit activity in physiological disease pathways of interest, and to develop purified forms of these proteins that are suitable for therapeutic application. A significant portion of the research that we are conducting involves new compounds and drug discovery methods, including our proprietary technology. Our drug discovery activities using our proprietary technology may not be successful in identifying product candidates that are useful in treating rare or more common diseases. Our research programs, including Project ORCA, may initially show promise in identifying potential product candidates, such as Stalaris, yet fail to yield product candidates for clinical development for a number of reasons, including:

- the research methodology used may not be successful in identifying appropriate potential product candidates; or
- potential product candidates may, on further study, be shown to have harmful side effects or other characteristics that indicate that they are unlikely to be medicines that will receive marketing approval and achieve market acceptance.

Research programs to identify new product candidates require substantial technical, financial and human resources. We may choose to focus our efforts and resources on a potential product candidate that ultimately proves to be unsuccessful. If we are unable to identify suitable product candidates for preclinical and clinical development and regulatory approval, we will not be able to generate product revenues, which would have an adverse impact on our business, prospects, financial condition and results of operations.

We may encounter difficulties enrolling patients in our clinical trials for a variety of reasons, including the limited number of patients who have the diseases for which our product candidates are being studied, which could delay or halt the clinical development of our product candidates.

Identifying and qualifying patients to participate in our ongoing and planned clinical trials of Resolaris and any other clinical trials that we may conduct for our product candidates is critical to our success. In particular, each of the conditions for which we currently plan to evaluate Resolaris is a rare disease with limited patient pools from which to draw for clinical trials. For example, while estimates of FSHD prevalence vary, studies exploring the topic have identified average prevalence rates of approximately one in 17,000. Applying this rate to the U.S. population, as of November 1, 2014, yields a domestic FSHD population of approximately 19,000. In addition, we estimate that LGMD affects an estimated 16,000 patients in the U.S., approximately 3,000 of whom have LGMD2B. The eligibility criteria for our clinical trials may further limit the pool of available participants in our trials. We may be unable to identify and enroll a sufficient number of patients with the disease in question and who meet the eligibility criteria for, and are willing to participate in, our clinical trials. Once enrolled, patients may decide or be required to discontinue from our clinical trials due to inconvenience, burden of trial requirements, adverse events associated with our product candidates or limitations required by trial protocols.

Our ability to identify, recruit enroll and maintain a sufficient number of patients, or those with required or desired characteristics to achieve diversity in a study, to complete our clinical trials in a timely manner may also be affected by other factors, including:

- proximity and availability of clinical trial sites for prospective patients;
- severity of the disease under investigation;
- design of the study protocol and the burdens to patients of compliance with our study protocols;
- perceived risks and benefits of the product candidate under study;
- availability of competing therapies and clinical trials for the patient populations and indications under study;
- efforts to facilitate timely enrollment in clinical trials;
- patient referral practices of physicians; and
- ability to monitor patients adequately during and after treatment.

We are initially focused on the development of Physiocrine-based therapeutics to treat rare conditions. We plan to seek initial marketing approval in the United States. We may not be able to initiate or continue clinical trials if we cannot enroll a sufficient number of eligible patients to participate in the clinical trials required by the FDA or other regulatory agencies. Our ability to successfully initiate, enroll and complete a clinical trial in any foreign country is subject to numerous risks unique to conducting business in foreign countries, including:

- difficulty in establishing or managing relationships with CROs and physicians;
- different requirements and standards for the conduct of clinical trials;
- our inability to locate qualified local consultants, physicians and partners; and
- the potential burden of complying with a variety of foreign laws, medical standards and regulatory requirements, including the regulation of pharmaceutical and biotechnology products and treatment.

Additionally, if patients are unwilling to participate in our clinical trials because of negative publicity from adverse events in our clinical trials or in the biotechnology or protein therapeutics industries or for other reasons, including competitive clinical trials for similar patient populations, the timeline for recruiting patients, conducting studies and obtaining regulatory approval of potential products may be delayed. These delays could result in increased costs, delays in advancing our product development or termination of our clinical trials altogether. If we have difficulty enrolling and maintaining a sufficient number of patients to conduct our clinical trials as planned for any reason, we may need to delay, limit or terminate ongoing or planned clinical trials, any of which would have an adverse effect on our business, prospects, financial condition and results of operations.

We may face manufacturing stoppages and other challenges associated with the clinical or commercial manufacture of our Physiocrine-based therapeutics.

All entities involved in the preparation of therapeutics for clinical trials or commercial sale, including our existing contracted development and manufacturing organizations (CDMOs) for our product candidates, are subject to extensive regulation. Components of a finished therapeutic product approved for commercial sale or use in late-stage clinical trials must be manufactured in accordance with cGMP. These regulations govern manufacturing processes and procedures (including record keeping) and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Poor control of production processes can lead to the introduction of contaminants or to inadvertent changes in the properties or stability of our product candidates that may not be detectable in final product testing. We or our CDMOs must supply all necessary documentation in support of a biologics license application, or BLA, or a new drug application, or NDA, on a timely basis and must adhere to the FDA's GLP and cGMP regulations enforced by the FDA through its facilities inspection program. The facilities and quality systems of our CDMOs and other CROs must pass a pre-approval inspection for compliance with applicable regulations as a condition of regulatory approval of our product candidates. In addition, the regulatory authorities may, at any time, audit or inspect a manufacturing facility involved with the preparation of our product candidates or the associated quality systems for compliance with the regulations applicable to the activities being conducted. If these facilities do not pass a pre-approval plant inspection, FDA approval of the products will not be granted.

The regulatory authorities also may, at any time following approval of a product for sale, audit the facilities in which the product is manufactured. If any such inspection or audit of our facilities or those of our CDMOs and CROs identifies a failure to comply with applicable regulations or if a violation of our product specifications or applicable regulations occurs independently of such an inspection or audit, we or the relevant regulatory authority may require remedial measures that may be costly or time-consuming for us or a third party to implement and that may include the temporary or permanent suspension of a clinical trial or commercial sales or the temporary or permanent closure of a facility. Any such remedial measures imposed upon us or third parties with whom we contract could materially harm our business.

If we or any of our CDMOs and CROs fail to maintain regulatory compliance, the FDA can impose regulatory sanctions including, among other things, refusal to approve a pending application for a new biologic product or drug product, or revocation of a pre-existing approval. Additionally, if supply from one approved manufacturer is interrupted, there could be a significant disruption in clinical or commercial supply. An alternative manufacturer would need to be qualified through a BLA or NDA supplement which could result in further delay. The regulatory agencies may also require additional studies if a new manufacturer is relied upon for commercial production. Switching manufacturers may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines.

In addition, the manufacture of Resolaris and any other Physiocrine-based therapeutics that we may develop presents challenges associated with biologics production, including the inherent instability of larger, more complex molecules and the need to ensure uniformity of the drug substance produced in different facilities or across different batches. We have changed cell lines for the production of Resolaris in connection with our engagement of a new CDMO to meet our projected needs for pivotal clinical trials and a commercial chemistry, manufacturing and controls specification, which may present production challenges or delays. The process of manufacturing biologics is extremely susceptible to product loss due to contamination, equipment failure or improper installation or operation of equipment, or vendor or operator error. Even minor deviations from normal manufacturing and distribution processes for any of our product candidates could result in reduced production yields, product defects, and other supply disruptions. Furthermore, although Physiocrines represent a class of proteins that may share immuno-modulatory properties in various physiological pathways, each Physiocrine has a different structure and may have unique manufacturing requirements that are not applicable across the entire class. For example, Fc fusion proteins, such as Stalaris, include an additional antibody domain to improve pharmacokinetic, or PK, characteristics, and may therefore require a more complex and time-consuming manufacturing process than other Physiocrines. Currently, we are producing our Stalaris molecule in *E.coli* by expression in inclusion bodies and refolding to recreate the native structure. The manufacturing processes for one of our product candidates may not be readily adaptable to other product candidates that we develop, and we may need to engage multiple third-party manufacturers to produce our product candidates. Any adverse developments affecting manufacturing operations for our product candidates may result in shipment delays, inventory shortages, lot failures, withdrawals or recalls or other interruptions in the supply of our drug substance and drug product which could delay the development of our product candidates. We may also have to write off inventory, incur other charges and expenses for supply of drug product that fails to meet specifications, undertake costly remediation efforts, or seek more costly manufacturing alternatives. Any manufacturing stoppage or delay, or any inability to consistently manufacture adequate supplies of our product candidates for our ongoing or planned clinical trials or on a commercial scale will harm our business, prospects, financial condition and results of operations.

Although the FDA and the European Commission have granted orphan drug designation to Resolaris for the treatment of FSHD and LGMD, we may not receive orphan drug designation for Resolaris in other jurisdictions or for other indications that we may pursue, or for any other product candidates we may develop under any new applications for orphan drug designation that we may submit, and any orphan drug designations that we have received or may receive may not confer marketing exclusivity or other expected commercial benefits.

The FDA and the European Commission have each granted orphan drug designations to Resolaris for the treatment of FSHD and for the treatment of LGMD. We may also apply for orphan drug designation in other territories and for other indications and product candidates. Orphan drug status confers up to ten years of marketing exclusivity in Europe, and up to seven years of marketing exclusivity in the United States, for a particular product in a specified indication. To date, we have been granted orphan drug designation for only one product candidate in the United States and the European Union for two indications. We cannot assure you that we will be able to obtain orphan drug designation, or rely on orphan drug or similar designations to exclude other companies from manufacturing or selling products using the same principal mechanisms of action for the same indications that we pursue beyond these timeframes. Furthermore, marketing exclusivity in Europe can be reduced from ten years to six years if the initial designation criteria have significantly changed since the market authorization of the orphan product. Even if we are the first to obtain marketing authorization for an orphan drug indication, there are circumstances under which a competing product may be approved for the same indication during the period of marketing exclusivity, such as if the later product is shown to be clinically superior to the orphan product, or if the later product is deemed a different product than ours. Further, the marketing exclusivity would not prevent competitors from obtaining approval of the same product candidate as ours for indications other than those in which we have been granted orphan drug designation, or for the use of other types of products in the same indications as our orphan product.

Even if we complete the necessary preclinical studies and clinical trials, we cannot predict when or if we will obtain regulatory approval to commercialize a product candidate, and the scope of any approval may be narrower than we expect.

We cannot commercialize a product until the appropriate regulatory authorities have reviewed and approved the product candidate. Even if our product candidates demonstrate safety and efficacy in clinical trials, the regulatory agencies may not complete their review processes in a timely manner, or we may not be able to obtain regulatory approval. Additional delays may result if an FDA Advisory Committee or regulatory authority recommends non-approval or restrictions on approval. In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action, or changes in regulatory agency policy during the period of product development, clinical trials and the review process. Regulatory agencies also may approve a product candidate for fewer or more limited indications than requested, may impose restrictions on dosing or may grant approval subject to the performance of post-marketing studies. In addition, regulatory agencies may not approve the labeling claims that are necessary or desirable for the successful commercialization of our product candidates.

Failure to obtain marketing approval in international jurisdictions would prevent our medicines from being marketed in such jurisdictions.

In order to market and sell our medicines in the European Union and many other jurisdictions, we must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing, and we have limited regulatory experience in many jurisdictions. The time required to obtain approval in one jurisdiction may differ substantially from that required to obtain approval in other jurisdictions. The regulatory approval process outside the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by one regulatory authority does not ensure approval by regulatory authorities in other countries or jurisdictions, and we may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our medicines in any market.

A breakthrough therapy or fast track designation by the FDA may not lead to expedited development or regulatory review or approval.

In October 2016 and January 2017, the FDA granted Resolaris fast track designations for the treatment of FSHD and LGMD2B, respectively. We may also seek, from time to time, breakthrough therapy or fast track designation for Resolaris for other indications and for any other product candidates that we may develop, although we may elect not to do so. A breakthrough therapy program is for a product candidate intended to treat a serious or life-threatening condition, and preliminary clinical evidence indicates that the product candidate may demonstrate substantial improvement on a clinically significant endpoint(s) over available therapies. A fast track program is for a product candidate that treats a serious or life-threatening condition, and nonclinical or clinical data demonstrate the potential to address an unmet medical need. The FDA has broad discretion whether or not to grant these designations. Accordingly, even if we believe a particular product candidate is eligible for breakthrough therapy or fast track designation, we cannot assure you that the FDA would decide to grant it. Even though we have received fast track designation for Resolaris for the treatment of FHSD and LGMD2B, or even if we receive breakthrough therapy or fast track designation of other indications or for our other product candidates, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw breakthrough therapy or fast track designation if it believes that the product no longer meets the qualifying criteria. In addition, the breakthrough therapy program is a relatively new program. As a result, we cannot be certain

whether any of our product candidates can or will qualify for breakthrough therapy designation. Our business may be harmed if we are unable to avail ourselves of these or any other expedited development and regulatory pathways.

Even if we obtain regulatory approval for a product candidate, our products will remain subject to regulatory scrutiny.

Even if Resolaris, Stalaris or any other product candidates that we discover and develop are approved, they will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping, conduct of post-marketing studies, and submission of safety, efficacy, and other post-market information, including both federal and state requirements in the United States and requirements of comparable foreign regulatory authorities.

Manufacturers and manufacturers' facilities are required to comply with extensive FDA, and comparable foreign regulatory authority, requirements, including ensuring that quality control and manufacturing procedures conform to cGMP regulations. As such, we and our contract manufacturers will be subject to continual review and inspections to assess compliance with cGMP and adherence to commitments made in any BLA, NDA, or marketing authorization application, or MAA. Accordingly, we and others with whom we work will need to continue to expend time, money, and effort in all areas of regulatory compliance, including manufacturing, production, and quality control.

Any regulatory approvals that we receive for our product candidates may be subject to limitations on the approved indicated uses for which the product may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials, and surveillance to monitor the safety and efficacy of the product candidate. We will be required to report certain adverse reactions and production problems, if any, to the FDA and comparable foreign regulatory authorities. If new safety issues emerge, we may be required to change our labeling. Any new legislation addressing drug safety or efficacy issues could result in delays in product development or commercialization, or increased costs to assure compliance.

We will have to comply with requirements concerning advertising and promotion for our products. Promotional communications with respect to prescription drugs are heavily scrutinized by the FDA, the Department of Justice, state attorneys general and comparable foreign regulatory authorities. For example, we may face claims associated with the use or promotion of our products for uses outside the scope of their approved label indications. Violations, including actual or alleged promotion of our products for unapproved, or off-label, uses are subject to enforcement letters, inquiries and investigations, and civil and criminal sanctions. Any actual or alleged failure to comply with labeling and promotion requirements may have a negative impact on our business. In the United States, engaging in impermissible promotion of our products for off-label uses can also subject us to false claims litigation under federal and state statutes, which can lead to civil and criminal penalties and fines and agreements that would materially restrict the manner in which we promote or distribute our drug products. These false claims statutes include the federal False Claims Act, which allows any individual to bring a lawsuit against a pharmaceutical company on behalf of the federal government alleging submission of false or fraudulent claims, or causing to present such false or fraudulent claims, for payment by a federal program such as Medicare or Medicaid. If the government prevails in the lawsuit, the individual will share in any fines or settlement funds. Since 2004, these False Claims Act lawsuits against pharmaceutical companies have increased significantly in volume and breadth, leading to several substantial civil and criminal settlements based on certain sales practices promoting off-label drug uses. This growth in litigation has increased the risk that a pharmaceutical company will have to defend a false claims action, pay settlement fines or restitution, agree to comply with burdensome reporting and compliance obligations, and be excluded from Medicare, Medicaid and other federal and state healthcare programs. If we do not lawfully promote our approved products, we may become subject to such litigation and, if we are not successful in defending against such actions, those actions could compromise our ability to become profitable.

The holder of an approved BLA, NDA or MAA must submit new or supplemental applications and obtain approval for certain changes to the approved product, product labeling, or manufacturing process. We could also be asked to conduct post-marketing clinical trials to verify the safety and efficacy of our products in general or in specific patient subsets. If original marketing approval were obtained through an accelerated approval pathway, we could be required to conduct a successful post-marketing clinical trial to confirm clinical benefit for our products. An unsuccessful post-marketing study or failure to complete such a trial could result in the withdrawal of marketing approval.

If a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, or disagrees with the promotion, marketing or labeling of a product, such regulatory agency may impose restrictions on that product or us, including requiring withdrawal of the product from the market. If we fail to comply with applicable regulatory requirements, a regulatory agency or enforcement authority may, among other things:

- issue untitled or warning letters;
- impose civil or criminal penalties;
- suspend or withdraw regulatory approval;

- suspend any of our ongoing clinical trials;
- refuse to approve pending applications or supplements to approved applications submitted by us;
- impose restrictions on our operations, including closing our contract manufacturers' facilities; or
- seize or detain products, or require or request a product recall.

Any government investigation of alleged violations of law could require us to expend significant time and resources in response, and could generate negative publicity. Any failure to comply with ongoing regulatory requirements may significantly and adversely affect our ability to commercialize and generate revenue from our products. If regulatory sanctions are applied or if regulatory approval is withdrawn, the value of our company and our operating results will be adversely affected.

Because of our focus on treatments for severe, rare diseases, Resolaris, Stalaris and other product candidates that we develop may be subject to requests for treatment use under individual patient INDs, which would present a variety of risks.

FDA regulations permit an investigational drug or biologic to be used for the treatment of an individual patient by a licensed physician under certain circumstances if the patient has a serious disease or condition, generally defined as a disease or condition associated with morbidity that has a substantial impact on day-to-day functioning. We believe that Resolaris, Stalaris and other product candidates that we develop may be susceptible to physician requests for use in these settings given the severity of the disease indications that we are targeting and the limited availability of approved and other investigational therapeutics for these indications. The treatment use of our product candidates under individual patient INDs would present a number of risks, including the following:

- The treatment use of our product candidates under individual patient INDs may be subject to less stringent or otherwise different protocols from our clinical trials, subjecting the patient to additional risk, which could negatively affect the perception of our product candidates among physicians, patients and regulators;
- The actual or perceived availability of a product candidate for use under individual patient INDs may impair patient enrollment in our clinical trials; and
- Any decision to make quantities of our product candidates available for use under individual patient INDs may impair our or our third-party manufacturers' ability to timely supply adequate quantities of our product candidates for our clinical trials.

Physicians may independently file individual patient INDs for Resolaris or, when in clinical trials, for Stalaris or one of our other product candidates. We may disagree with a physician's or the FDA's conclusion that our product candidate is suitable for evaluation under a particular individual patient IND, and any decision by us not to make our product candidate available for evaluation under this setting may subject us to negative publicity or market perception.

As part of the recently enacted 21st Century Cures Act, or Cures Act, as the manufacturer of an investigational drug for a serious disease or condition, we will be required to make available, such as by posting on our website, our policy on evaluating and responding to requests for individual patient access to such investigational drug. This requirement applies on the later of 60 calendar days after the date of enactment of the Cures Act or the first initiation of a Phase 2 or Phase 3 trial of the investigational drug.

Risks related to our financial condition 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 are a clinical stage biotherapeutics company, and we have not yet generated any revenues from product sales. We have incurred net losses in each year since our inception in 2005, including net losses of $57.9 million, $48.0 million and $24.4 million for the years ended December 31, 2016, 2015 and 2014, respectively. As of December 31, 2016, we had an accumulated deficit of $216.0 million.

We have devoted most of our financial resources to research and development, including our clinical and preclinical development activities. To date, we have financed our operations primarily through the sale of equity securities and convertible debt and through commercial bank debt. The amount of our future net losses will depend, in part, on the rate of our future expenditures and our ability to obtain funding through equity or debt financings, grant funding or strategic collaborations. We have not commenced pivotal clinical trials for any product candidate and it will be several years, if ever, before we have a product candidate ready for commercialization. Even if we obtain regulatory approval to market a product candidate, our future revenues will depend upon the size of any markets in which our product candidates have received approval, and our ability to achieve sufficient market acceptance, reimbursement from third-party payors and adequate market share for our product candidates in those markets. However, even if we obtain adequate market share for our product candidates, because the potential markets in which our product candidates may ultimately receive regulatory approval are very small, we may never become profitable despite obtaining such market share and acceptance of our products.

We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future. We anticipate that our expenses will increase substantially if and as we:

- continue our research and preclinical and clinical development of Resolaris, Stalaris or any other product candidates that we may develop;
- initiate and conduct any additional preclinical studies, clinical trials or other studies for Resolaris, Stalaris and any other product candidates that we may develop;
- further develop the manufacturing process for our product candidates;
- change or add additional manufacturers, including manufacturers of quantities of drug substance suitable for pivotal clinical trials and commercialization;
- seek regulatory approvals for our product candidates that successfully complete clinical trials;
- establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain marketing approval;
- seek to identify and validate additional product candidates;
- make milestone or other payments under our in-license agreements;
- maintain, protect and expand our portfolio of owned and in-licensed intellectual property;
- acquire or in-license other product candidates and technologies;
- attract and retain skilled personnel;
- create additional infrastructure to support our operations as a public company and our product development and planned future commercialization efforts; and
- experience any delays or encounter challenges with any of the above.

The net losses we incur may fluctuate significantly from quarter to quarter and year to year, such that a period-to-period comparison of our results of operations may not be a good indication of our future performance. In any particular quarter or quarters, our operating results could be below the expectations of securities analysts or investors, which could cause our stock price to decline.

We have never generated any revenue from product sales and may never be profitable.

Our ability to generate revenue and achieve profitability depends on our ability, alone or with strategic collaboration partners, to successfully complete the development of, and obtain the regulatory approvals necessary to commercialize, Resolaris and any other product candidates that we may develop. We do not anticipate generating revenues from product sales for the foreseeable future, if ever. Our ability to generate future revenues from product sales depends heavily on our success in:

- completing research, preclinical development and clinical development of Resolaris, Stalaris and other product candidates, potentially with a partner in one or more of our programs;
- seeking and obtaining regulatory approvals for product candidates for which we complete clinical trials;
- developing a sustainable, scalable, reproducible, and transferable manufacturing process for Resolaris, Stalaris and any other product candidates that we may develop;
- establishing and maintaining supply and manufacturing relationships with third parties that can provide products and services that are adequate in both amount and quality to support clinical development and the market demand for our product candidates, if approved;
- launching and commercializing product candidates for which we obtain regulatory approval, either by collaborating with a partner or, if launched independently, by establishing a sales force, marketing and distribution infrastructure;
- maintaining, protecting and expanding our portfolio of intellectual property rights, including patents, trademarks, trade secrets and know-how;
- obtaining market acceptance of Physiocrine therapeutics and our product candidates as viable treatment options for our target indications;
- addressing any competing technological and market developments;
- implementing additional internal systems and infrastructure, as needed;

- identifying and validating new Physiocrine therapeutic product candidates;
- attracting, hiring and retaining qualified personnel; and
- negotiating favorable terms in any licensing, collaboration or other arrangements into which we may enter.

Even if Resolaris, Stalaris or any of the other product candidates that we may develop is approved for commercial sale, we anticipate incurring significant costs associated with commercializing any approved product candidate. Our expenses could increase beyond expectations if we are required by the FDA or other regulatory agencies, domestic or foreign, to perform clinical trials and other studies in addition to those that we currently anticipate. In cases where we are successful in obtaining regulatory approvals to market one or more of our product candidates, our revenue will be dependent, in part, upon the size of the markets in the territories for which we gain regulatory approval, the accepted price for the product, the ability to get reimbursement at any price, the competition we face, and whether we own the commercial rights for that territory. If the number of our addressable rare disease patients is not as significant as we estimate, the indication approved by regulatory authorities is narrower than we expect, or the reasonably accepted population for treatment is narrowed by competition, physician choice or treatment guidelines, we may not generate significant revenue from sales of such products, even if approved. Even if we are able to generate revenues from the sale of any approved products, we may not become profitable and may need to obtain additional funding to continue operations.

We will likely need to raise additional capital or enter into strategic partnering relationships to fund our operations. Failure to obtain this necessary capital when needed may force us to delay, limit or terminate our product development efforts or other operations.

We are currently advancing Resolaris through clinical development, preparing to initiate clinical development for Stalaris and conducting preclinical development activities directed at the identification and selection of additional Physiocrine-based therapeutic candidates, including Project ORCA. The development of protein therapeutics is expensive, and we expect our research and development expenses to increase substantially in connection with our ongoing activities.

As of December 31, 2016, our cash, cash equivalents and available-for-sale investments were approximately $76.1 million. We expect that our existing cash, cash equivalents and available-for-sale investments will be sufficient to fund our current operations through at least the next 12 months. However, our operating plan may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned, through public or private equity or debt financings, government or other third-party funding, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements or a combination of these approaches. Our future funding requirements will depend on many factors, including but not limited to:

- the scope, rate of progress, results and cost of our clinical trials, nonclinical testing, and other related activities;
- the cost of manufacturing clinical supplies, and establishing commercial supplies, of our product candidates and any products that we may develop;
- the number and characteristics of product candidates that we pursue;
- the cost, timing, and outcomes of regulatory review of our product candidates;
- the cost and timing of establishing sales, marketing, and distribution capabilities; and
- the terms and timing of any collaborative, licensing, and other arrangements that we may establish, including any required milestone and royalty payments thereunder.

In any event, we will require additional capital to complete additional clinical trials, including larger, pivotal clinical trials, to obtain regulatory approval for, and to commercialize, our product candidates.

For some of our programs and product candidates, we may decide to enter into strategic partnerships, including collaborations with pharmaceutical and biotechnology companies, to enhance and accelerate the development and potential commercialization of our product candidates. We face significant competition in seeking appropriate partners, and the negotiation process is time-consuming and complex. Moreover, we may not be successful in our efforts to establish a strategic partnership or other collaborative arrangement for any of our product candidates and programs for a variety of reasons, including strategic fit with partners and differences in analysis of commercial value and regulatory risk. We may not be able to negotiate strategic partnerships on a timely basis, on acceptable terms or at all. We are unable to predict when, if ever, we will enter into any strategic partnership because of the numerous risks and uncertainties associated with establishing strategic partnerships. Even if we are successful in our efforts to establish strategic partnerships, the terms that we agree upon may not be favorable to us and we may not be able to maintain such strategic partnerships if, for example, we encounter unfavorable results or delays during development or approval of a product candidate or sales of an approved product are lower than expectations.

Raising funds in the current economic environment may present additional challenges. Even if we believe we have sufficient funds for our current or future operating plans, we may seek additional capital if market conditions are favorable or if we have specific strategic considerations. If we are unable to obtain funding on a timely basis, we may be required to significantly curtail, delay or discontinue one or more of our research or development programs or the commercialization of any product candidates, or we may be unable to expand our operations, maintain our current organization and employee base or otherwise capitalize on our business opportunities, as desired, which could materially affect our business, financial condition and results of operations.

Raising additional capital may cause dilution to our existing stockholders, restrict our operations, require us to relinquish rights to our technologies or product candidates on terms unfavorable to us and divert management's attention from our product development activities.

The terms of any financing may adversely affect the holdings or the rights of our stockholders and the issuance of additional securities, whether equity or debt, by us, or the possibility of such issuance, may cause the market price of our shares to decline. The sale of additional equity or convertible securities would cause dilution to all of our stockholders. The incurrence of additional indebtedness would increase our fixed payment obligations and may require us to agree to certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. We may seek funds through arrangements with collaborative partners or otherwise at an earlier stage than desirable and we may be required to relinquish rights to some of our technologies or product candidates or otherwise agree to terms unfavorable to us, any of which may have a material adverse effect on our business, operating results and prospects. In addition, any fundraising efforts may divert our management from their day-to-day activities, which may adversely affect our ability to develop and commercialize our product candidates.

We have a significant amount of debt that may cause risks that could adversely affect our business, operating results and financial condition.

On November 18, 2016, we entered into a loan and security agreement, or Loan Agreement, for a term loan with Silicon Valley Bank and Solar Capital Ltd., which we refer to as the Term Loan. The Loan Agreement provides up to $20 million principal in new term loans, $10 million of which was funded on November 18, 2016. The remaining $10 million is available for draw as follows: $5 million is available until June 30, 2017 and $5 million is available until December 31, 2017, each at the Company's discretion, subject to achievement of certain financial and clinical milestones. The Term Loan is secured by substantially all of our assets and the assets of our domestic subsidiaries, except that the collateral does not include any intellectual property held by us or our respective subsidiaries or more than 65% of any voting securities in our foreign subsidiaries owned or held of record by us. However, pursuant to the terms of a negative pledge arrangement, we have agreed not to encumber any of the intellectual property of ours or our subsidiaries. The level and nature of our indebtedness could, among other things:

- make it difficult for us to obtain any necessary financing in the future;
- limit our flexibility in planning for or reacting to changes in our business;
- reduce funds available for use in our operations and corporate development initiatives;
- impair our ability to incur additional debt because of financial and other restrictive covenants or the liens on our assets that secure our current debt;
- hinder our ability to raise equity capital, because in the event of a liquidation of our business, debt holders receive a priority before equity holders;
- make us more vulnerable in the event of a downturn in our business; and
- place us at a possible competitive disadvantage relative to less leveraged competitors and competitors that have better access to capital resources.

In addition, if we do not meet certain conditions set forth in the Loan Agreement, we will not be able to draw the remaining $10 million available under the Term Loan, which could materially harm our financial condition. We may also incur significantly more debt in the future, which will increase each of the risks described above related to our indebtedness.

The Loan Agreement for the Term Loan contains operating covenants that may restrict our business and financing activities.

The Loan Agreement restricts, among other things, our ability to:

- convey, sell, lease, transfer, assign or otherwise dispose of certain of our assets;
- engage in any business other than the businesses we currently engage in or reasonably related thereto or reasonable extensions thereof;

- undergo certain change of control events;
- create, incur, assume, or be liable with respect to certain indebtedness;
- grant certain liens;
- pay dividends and make certain other restricted payments;
- make certain investments;
- enter into any material transactions with any affiliates, with certain exceptions; or
- permit certain of our subsidiaries to hold or maintain certain assets in excess of certain specified amounts.

The operating restrictions and covenants in the Loan Agreement, as well as any future financing agreements that we may enter into, may restrict our ability to finance our operations, engage in business activities or expand or fully pursue our business strategies. Our ability to comply with these covenants may be affected by events beyond our control and we may not be able to meet those covenants. A breach of any of the covenants under the Loan Agreement could result in a default under the Loan Agreement, which could cause all of the outstanding indebtedness under the Term Loan to become immediately due and payable.

Risks related to our reliance on third parties

We rely, and expect to continue to rely, on third parties to conduct some or all aspects of our product manufacturing, protocol development, research and preclinical and clinical testing, and these third parties may not perform satisfactorily.

We currently rely, and expect to continue to rely, on third parties to conduct some or all aspects of product manufacturing, protocol development, research and preclinical and clinical testing with respect to our product candidates. Any of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements, it could delay our product development activities. Our reliance on these third parties for research and development activities reduces our control over these activities but does not relieve us of our responsibility to ensure compliance with all required regulations and study protocols. For example, for Resolaris, Stalaris and any other product candidates that we develop and commercialize on our own, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the applicable study plan and protocols and cGCPs so long as we continue to develop and commercialize on our own.

If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our research and development activities, including clinical trials, in accordance with regulatory requirements or our stated study plans and protocols, we will not be able to complete, or may be delayed in completing, the preclinical studies and clinical trials required to support future BLA or NDA submissions and approval of our product candidates.

We rely on third parties to manufacture our clinical supply of Resolaris, and we intend to rely on third parties to produce nonclinical, clinical and commercial supplies of Stalaris and any future product candidate.

We do not have, nor do we plan to acquire, the infrastructure or capability internally to manufacture our nonclinical and clinical quantities of our product candidates, and we lack the internal resources and capability to manufacture any of our product candidates on a clinical or commercial scale. Reliance on CDMOs and CROs, entails risks to which we would not be subject if we manufactured the product candidates ourselves, including:

- the inability to negotiate manufacturing agreements with third parties under commercially reasonable terms;
- reduced control as a result of using third-party CDMOs and CROs for all aspects of manufacturing activities;
- termination or nonrenewal of manufacturing agreements with third parties in a manner or at a time that is costly or damaging to us; and
- disruptions to the operations of our CDMOs, CROs or suppliers caused by conditions unrelated to our business or operations, including the insolvency or bankruptcy of the CDMOs, CROs or supplier.

Any of these events could lead to clinical trial delays or failure to obtain regulatory approval, or impact our ability to successfully commercialize future products. Some of these events could be the basis for FDA action, including injunction, recall, seizure or total or partial suspension of production.

Additionally, each CDMO may require licenses to manufacture our product candidates or components thereof if the applicable manufacturing processes are not owned by the CDMO or in the public domain, and we may be unable to transfer or sublicense the intellectual property rights we may have with respect to such activities. These factors could cause the delay of clinical development, regulatory submissions, required approvals or commercialization of our product candidates, cause us to incur higher costs and prevent us from commercializing our products successfully.

We currently rely on a single CDMO for bulk drug substance for Resolaris for our projected needs for ongoing and anticipated pivotal clinical trials. Subject to the satisfactory completion of process validation and other requirements, we may contract with this CDMO for larger scale commercial manufacturing. Similarly, we currently rely on a single CDMO for process development and scale-up of Stalaris. We do not have long-term contracts with our CDMOs, and our CDMOs may terminate their agreements with us for a variety of reasons including technical issues or our material breach of our obligations under the applicable agreement. Furthermore, our CDMOs may reallocate resources away from the production of our product candidates if we delay manufacturing under certain circumstances, and the manufacturing facilities in which our product candidates are made could be adversely affected by earthquakes and other natural disasters, labor shortages, power failures, and numerous other factors. If our CDMOs fail to meet contractual requirements, and we are unable to secure one or more replacement CDMOs capable of production at a substantially equivalent cost, our clinical development activities may be delayed, or we could lose potential revenue. Manufacturing biologic drugs is complicated and tightly regulated by the FDA and comparable regulatory authorities around the world, and although alternative CDMOs with the necessary manufacturing and regulatory expertise and facilities exist, it could be expensive and take a significant amount of time to arrange for alternative CDMOs, transfer manufacturing procedures to these alternative CDMOs, and demonstrate comparability of material produced by such new CDMOs. New CDMOs of any product would be required to comply with applicable regulatory requirements. These CDMOs may not be able to manufacture our product candidates at costs, or in quantities, or in a timely manner necessary to complete the clinical development of our product candidates or make commercially successful products.

We rely, and expect to continue to rely, on third parties to conduct, supervise and monitor our clinical trials, and if these third parties perform in an unsatisfactory manner, it may harm our business.

We have relied, and expect to continue to rely, on third-party CROs, clinical investigators and clinical trial sites to ensure our clinical trials are conducted properly and on time. While we have and will continue to enter into agreements governing their activities, we will have limited influence over their actual performance. We will control only certain aspects of our CROs' activities. Nevertheless, we will be responsible for ensuring that each of our clinical trials is conducted in accordance with the applicable protocol, legal and regulatory requirements, and scientific standards, and our reliance on the CROs does not relieve us of our regulatory responsibilities.

We and our investigators and CROs are required to comply with GCPs for conducting, recording and reporting the results of clinical trials to assure that the data and reported results are credible and accurate and that the rights, integrity and confidentiality of clinical trial participants are protected. The FDA enforces GCPs through periodic inspections of study sponsors, principal investigators and clinical trial sites. If we or our investigators and CROs fail to comply with applicable GCPs, the clinical data generated in our future clinical trials may be deemed unreliable and the FDA may require us to perform additional unanticipated clinical trials before approving any marketing applications. Upon inspection, the FDA may determine that our clinical trials did not comply with GCPs. In addition, our future clinical trials will require a sufficient number of test subjects to evaluate the safety and effectiveness of our product candidates. Accordingly, if our investigators and CROs fail to comply with these regulations or fail to recruit a sufficient number of patients, we may be required to repeat such clinical trials, which would delay the regulatory approval process.

Our investigators and CROs are not our employees, and we are therefore unable to directly monitor whether or not they devote sufficient time and resources to our clinical and nonclinical programs. They may also have relationships with other commercial entities, including our competitors, for whom they may also be conducting clinical trials or other drug development activities that could harm our competitive position. If our investigators or CROs do not successfully carry out their contractual duties or obligations, fail to meet expected deadlines, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements, or for any 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 product candidates. As a result, our financial results would be harmed, our costs could increase, our ability to generate revenues could be delayed and the commercial prospects for our product candidates will be adversely affected.

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.

We rely on third parties to manufacture our product candidates, and we collaborate with various academic institutions in the development of our discovery engine for therapeutic applications of Physiocrines. In connection with these activities, we are required, at times, to 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, collaborative research agreements, consulting agreements or other similar agreements with our collaborators, advisors, employees 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, such as 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 a material adverse effect on our business, prospects, financial condition and results of operations.

In addition, these agreements typically restrict the ability of our collaborators, advisors, employees and consultants to publish data potentially relating to our trade secrets. Our academic collaborators typically have rights to publish data, provided that we are notified in advance and may delay publication for a specified time in order to secure intellectual property rights to which we are entitled arising from the collaboration. In other cases, publication rights are controlled exclusively by us, although in some cases we may share these rights with other parties. We also conduct joint research and development programs that may require us to share trade secrets under the terms of our research and development partnerships or similar agreements. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of these agreements, independent development or publication of information including our trade secrets in cases where we do not have proprietary or otherwise protected rights at the time of publication. A competitor's discovery of our trade secrets would impair our competitive position and have an adverse impact on our business, prospects, financial condition and results of operations.

Risks related to the commercialization of our product candidates

If we are unable to establish sales and marketing capabilities or enter into agreements with third parties to market and sell our product candidates, we may be unable to generate any revenues.

We do not currently have any infrastructure for the sales, marketing and distribution of pharmaceutical products. In order to market our product candidates, if approved by the FDA or any other regulatory body, we must build our sales, marketing, managerial and other non-technical capabilities or make arrangements with third parties to perform these services. There are risks involved with both establishing our own sales and marketing capabilities and entering into arrangements with third parties to perform these services. For example, recruiting and training a sales force is expensive and time consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. This may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize our medicines on our own include:

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future medicines;
- the lack of complementary medicines to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we enter into arrangements or collaborations with third parties to perform sales, marketing and distribution services, our product revenues or the profitability of these product revenues to us are likely to be lower than if we were to market and sell any medicines that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell and market our product candidates or may be unable to do so on terms that are favorable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our medicines effectively. If we do not establish sales and marketing capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing our product candidates.

We rely on third-party manufacturers to produce Resolaris, Stalaris and any other product candidates that we may develop, but we have not entered into agreements with any such manufacturers to support commercialization.

We have not yet secured manufacturing capabilities for commercial quantities of Resolaris, Stalaris or any other product candidates. Although we intend to rely on third-party manufacturers for commercialization, we have only entered into agreements with such manufacturers to support our human proof-of-concept clinical trials. We have not yet entered into a long-term commercial supply agreement to support full scale commercial production, and we or our contract manufacturers may be unable to process validation activities necessary to enter into commercial supply agreements or otherwise negotiate agreements with the manufacturers to support our commercialization activities at commercially reasonable terms.

We may run into technical or scientific issues related to development or manufacturing that we may be unable to resolve in a timely manner or with available funds. If we or our manufacturing partners are unable to scale the manufacturing process to produce commercial quantities of our product candidates, or our manufacturing partners do not pass required regulatory pre-approval inspections, our commercialization efforts will be harmed.

In addition, any significant disruption in our relationships with our manufacturers could harm our business. There are a relatively small number of potential manufacturers for Resolaris, Stalaris and any other product candidates that we may develop, and such manufacturers may not be able to supply our drug products at the times we need them or on commercially reasonable terms. Any disruption to our relationship with our current manufacturers and any manufacturers that we contract with in the future will result in delays in our ability to complete the clinical development of, or to commercialize, Resolaris, Stalaris and any other product candidates we may develop, and may require us to incur additional costs.

We face intense competition and rapid technological change and the possibility that our competitors may develop therapies that are more advanced or effective than ours, which may adversely affect our financial condition and our ability to successfully commercialize our product candidates.

We are engaged in the development of medicines for severe, rare diseases, which is a competitive and rapidly changing field. We have competitors both in the United States and internationally, including major multi-national pharmaceutical companies, biotechnology companies and universities and other research institutions. In the area of rare myopathies with an immune component, we expect to face competition from a number of companies, academic institutions and other organizations, including Sarepta Therapeutics, PTC Therapeutics, Inc., Marathon Pharmaceuticals, Santhera Pharmaceuticals, Italfarmaco S.p.A, Summit Therapeutics, Catabasis Pharmaceuticals, Inc., FibroGen, Inc., F. Hoffmann-La Roche AG, Bristol Myers Squibb, Milo Biotechnology, LLC, Nobelpharma Co. Ltd., Pfizer, Inc., and Ultragenyx Pharmaceuticals, that are engaged in the clinical development of therapeutics to address muscle loss and muscle weakness in a variety of indications. More specifically, in the area of LGMD, we are aware of a number of academic institutions engaged in the clinical development of therapeutics, including Genethon, a not-for-profit research laboratory created by the Association Française contre les Myopathies, or French Muscular Dystrophy Association, which has completed an experimental Phase 1 clinical trial in LGMD2C using gene therapy; Nationwide Children's Hospital, which is currently conducting a Phase 1/2a clinical trial of an AAV vector to transport the alpha-sarcoglycan gene into muscles in LGMD2D; and NeuroGen Brain and Spine Institute in India, which is currently conducting a Phase 1 clinical trial in an unspecified form of LGMD using stem cell therapy. In addition, Pfizer currently has a program Domagrozumab (PF-06252616) which is in Phase 1b/2 clinical trials for the treatment of LGMD2I as well as a Phase 2 program for DMD. Although there are currently no approved products for the treatment of FSHD, Acceleron Pharma Inc. is developing a clinical candidate, ACE-083, a locally acting protein therapeutic designed to increase muscle mass and strength in patients with neuromuscular disorders and other diseases characterized by a loss of muscle function, including FSHD in which it initiated a Phase 2 trial in the fourth quarter of 2016. In addition, Facio Therapies, Novogen, Fulcrum Therapeutics, Ultragenyx Pharmaceuticals, Inc. and Idera Pharmaceuticals, Inc. are developing chemical compounds that may repress one of the causal genes responsible for FSHD. In the area of DMD, two therapies have been approved in the last 12 months: Exondys 51 from Sarepta and Emflaza from Marathon Pharmaceuticals. Marathon Pharmaceuticals and PTC Therapeutics, Inc. recently announced entering an asset purchase agreement whereby PTC Therapeutics, Inc. will acquire all rights to Emflaza.Exondys 51 is an antisense oligonucleotide indicated for the treatment of DMD in patients who have a confirmed mutation of the DMD gene that is amenable to exon 51 skipping. Many larger companies, universities and private and public research institutions are also actively engaged in the development of therapeutics to address muscle loss and muscle weakness in a variety of indications.

We may also face competition from numerous companies in the field of RPICs, including several companies that currently market Esbriet (pirfenidone) and Ofev (nintedanib), both of which were approved by the FDA for the treatment of ILD in October 2014.

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. Competition may increase further as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these industries. Our competitors may succeed in developing, acquiring or licensing on an exclusive basis, products that are more effective, safer, more convenient or less costly than any product candidate that we may develop, or achieve earlier patent protection, regulatory approval, product commercialization and market penetration than us. Additionally, technologies developed by our competitors may render our potential product candidates uneconomical or obsolete, and we may not be successful in marketing our product candidates against competitors.

Even if we are successful in achieving regulatory approval to commercialize a product candidate faster than our competitors, we may face competition from biosimilars due to the changing regulatory environment. In the United States, the Biologics Price Competition and Innovation Act of 2009 created an abbreviated approval pathway for biological products that are demonstrated to be "highly similar," or biosimilar, to or "interchangeable" with an FDA-approved biological product. This new pathway could allow competitors to reference data from biological products already approved after 12 years from the time of approval. In Europe, the European Commission has granted marketing authorizations for several biosimilars pursuant to a set of general and product class-specific guidelines for biosimilar approvals issued over the past few years. In Europe, a competitor may reference data from biological products already approved, but will not be able to get on the market until ten years after the time of approval. This ten year period will be extended to 11 years if, during the first eight of those ten years, the marketing authorization holder obtains an approval for one or more new therapeutic indications that bring significant clinical benefits compared with existing therapies. In addition, companies may be developing biosimilars in other countries that could compete with our products. If competitors are able to obtain marketing approval for biosimilars referencing our products, our products may become subject to competition from such biosimilars, with the attendant competitive pressure and consequences. Expiration or successful challenge of our applicable patent rights could also trigger competition from other products, assuming any relevant exclusivity period has expired.

Finally, as a result of the expiration or successful challenge of our patent rights, we could face more litigation with respect to the validity or scope of patents relating to our competitors' products. The availability of our competitors' products could limit the demand, and the price we are able to charge, for any products that we may develop and commercialize.

The commercial success of any current or future product candidate will depend upon the degree of market acceptance by physicians, patients, third-party payors and others in the medical community.

Even with the requisite approval from the FDA and comparable foreign regulatory authorities, the commercial success of our product candidates will depend in part on the medical community, patients, and third-party payors accepting our product candidates as medically useful, cost-effective, and safe. Any product that we bring to the market may not gain market acceptance by physicians, patients, third-party payors and others in the medical community. If these products do not achieve an adequate level of acceptance, we may not generate significant product revenue and may not become profitable. The degree of market acceptance of these product candidates, if approved for commercial sale, will depend on a number of factors, including:

- the potential efficacy and potential advantages over alternative treatments;
- the prevalence and severity of any side effects, including any limitations or warnings contained in a product's approved labeling;
- the prevalence and severity of any side effects resulting from the administration of our product candidates by injection;
- the clinical indications for which approval is granted;
- relative convenience and ease of administration;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- the strength of marketing and distribution support and timing of market introduction of competitive products;
- publicity concerning our products or competing products and treatments; and
- the availability of sufficient third-party insurance coverage or reimbursement.

Even if a potential product displays a favorable efficacy and safety profile in preclinical studies and clinical trials, market acceptance of the product will not be known until after it is launched. Our efforts to educate the medical community and third-party payors on the benefits of the product candidates may require significant resources and may never be successful. Such efforts to educate the marketplace may require more resources than are required by the conventional technologies marketed by our competitors, and our competitors may have substantially greater resources or brand recognition to effectively market their products. If our product candidates are approved but fail to achieve an adequate level of acceptance by physicians, patients, third-party payors, and others in the medical community, we will not be able to generate sufficient revenue to become or remain profitable.

The insurance coverage and reimbursement status of newly-approved products is uncertain. Failure to obtain or maintain adequate coverage and reimbursement for new or current products could limit our ability to market those products and decrease our ability to generate revenue.

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 medicines are typically made by the Centers for Medicare & Medicaid Services, or CMS, an agency within the U.S. Department of Health and Human Services, as CMS decides whether and to what extent a new medicine will be covered and reimbursed under Medicare. Private payors often follow CMS with respect to coverage policy and payment limitations in setting their own reimbursement policies. It is difficult to predict what CMS will decide with respect to reimbursement for fundamentally novel products such as ours, as there is no body of established practices and precedents for these new products. Reimbursement agencies in Europe may be more conservative than CMS. For example, a number of cancer drugs have been approved for reimbursement in the United States, but have not been approved for reimbursement in certain European countries. There may be significant delays in obtaining reimbursement for newly approved medicines, and our inability to promptly obtain coverage and profitable payment rates from third-party payors for any approved medicines could have a material adverse effect on our business, prospects, financial condition and results of operations.

Outside the United States, international sales 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 has and will continue to put pressure on the pricing and usage of our product candidates. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. In general, the prices of medicines under such systems are substantially lower than in the United States. Other countries allow companies to fix their own prices for medicines, 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 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. Net prices for medicines may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that currently restrict imports of medicines from countries where they may be sold at lower prices than in the United States.

Moreover, increasing efforts by governmental and third-party payors, in the United States and abroad, to cap or reduce healthcare costs may cause such organizations to limit both coverage and level of reimbursement for new products 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 product candidates, due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative changes, including the potential repeal and replacement of the Affordable Care Act. 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.

In addition, drug prices are under significant scrutiny in the markets in which our products may be sold. Drug pricing and other health care costs continues to be subject to intense political and societal pressures which we anticipate will continue and escalate on a global basis. As a result, our business and reputation may be harmed, our stock price may be adversely impacted and experience periods of volatility, we may have difficulty raising funds and our results of operations may be adversely impacted.

If the market opportunities for our product candidates are smaller than we believe they are, our revenues may be adversely affected and our business may suffer. Because the target patient populations of our product candidates are small, we must be able to successfully identify patients and capture a significant market share to achieve and maintain profitability.

We focus our research and product development on treatments for rare diseases. Given the small number of patients who have the diseases that we are targeting, it is critical to our ability to grow and become profitable that we continue to successfully identify patients with these rare diseases. Our projections of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with our product candidates, are based on our beliefs and estimates. These estimates have been derived from a variety of sources, including the scientific literature, surveys of clinics, patient foundations, or market research, and may prove to be incorrect. New studies may change the estimated incidence or prevalence of these diseases. The number of patients may turn out to be lower than expected. The effort to identify patients with diseases we seek to treat is in early stages, and we cannot accurately predict the number of patients for whom treatment might be possible. Additionally, the potentially addressable patient population for each of our product candidates may be limited or may not be amenable to treatment with our product candidates, and new patients may become increasingly difficult to identify or gain access to, which would adversely affect our results of operations and our business. Further, even if we obtain significant market share for our product candidates, because the potential target populations are very small, we may never achieve profitability despite obtaining such significant market share.

Our target patient populations are relatively small, and there is currently no standard of care treatment directed at some of our target indications, such as FSHD and LGMD2B. As a result, the pricing and reimbursement of our product candidates, if approved, is uncertain, but must be adequate to support commercial infrastructure. If we are unable to obtain adequate levels of reimbursement, our ability to successfully market and sell our product candidates will be adversely affected. The manner and level at which reimbursement is provided for services related to our product candidates (e.g., for administration of our product to patients) is also important. Inadequate reimbursement for such services may lead to physician resistance and adversely affect our ability to market or sell our products.

Risks related to our intellectual property

If we are unable to obtain, maintain or protect intellectual property rights related to our product candidates, or if the scope of such intellectual property protection is not sufficiently broad, we may not be able to compete effectively in our markets.

We rely upon a combination of patents, trade secret protection and confidentiality agreements to protect the intellectual property related to our technologies and product candidates. Our success depends in large part on our and our licensors' abilities to obtain and maintain patent and other intellectual property protection in the United States and in other countries for our proprietary technology and product candidates.

We have sought to protect our proprietary position by filing patent applications in the United States and abroad related to our novel technologies and product candidates that are important to our business. This 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 or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection.

The patentability of inventions, and the validity, enforceability and scope of patents in the biotechnology and pharmaceutical fields involves complex legal and scientific questions and can be uncertain. As a result, patent applications that we own or in-license may not issue as patents with claims that cover our product candidates, or at all, in the United States or in foreign countries for many reasons. For example, there is no assurance that we were the first to invent or the first to file patent applications in respect of the inventions claimed in our patent applications or that our patent applications claim patentable subject matter. We may also be unaware of potentially relevant prior art relating to our patents and patent applications, and this prior art, if any, may be used by third parties as grounds to seek to invalidate a patent or to prevent a patent from issuing from a pending patent application. Even if patents do successfully issue and even if such patents disclose aspects of our product candidates, third parties may challenge their validity, enforceability or scope, which may result in such patents being narrowed or invalidated. Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property, provide exclusivity for our product candidates or prevent others from designing around our claims. If the breadth or strength of protection provided by the patents and patent applications we hold, license or pursue with respect to our product candidates is threatened, it could threaten our ability to commercialize our product candidates. Further, if we encounter delays in our clinical trials, 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 were the first to file any patent application related to our product candidates. Changes to the patent laws in the United States and other jurisdictions could also diminish the value of our patents and patent applications or narrow the scope of our patent protection. Any of these outcomes could impair our ability to prevent competition from third parties, which may have an adverse impact on our business.

If the patent applications we own or have in-licensed that relate to our programs or product candidates do not issue as patents, if their breadth or strength of protection is threatened, or if they fail to provide exclusivity for our product candidates, it could dissuade companies from collaborating with us to develop product candidates, and threaten our ability to commercialize future products. We cannot offer any assurances about which, if any, patents will issue, the breadth of any such patents 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 licensed to us could deprive us of rights necessary for the successful commercialization of any product candidates that we may develop. In addition, patents have a limited term. In the United States, the natural expiration of a patent is generally 20 years after it is filed. Although various extensions may be available, the life of a patent, and the protection it affords, is limited. Even if a patent does issue for any of our pending patent applications, possible delays in regulatory approvals could mean that the period of time during which we could market a product candidate under patent protection could be reduced from what we generally would expect. Since patent applications in the United States and most other countries are confidential for a period of time after filing, and some remain so until issued, we cannot be certain that we were the first to file any patent application related to a product candidate. Furthermore, if third parties have filed such patent applications, an interference proceeding in the United States can be initiated by a third party to determine who was the first to invent any of the subject matter covered by the patent claims of our applications. Even if patents covering aspects of our product candidates are obtained, once the patent life has expired for a product, we may be open to competition from generic medications.

In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable or that we elect not to patent, processes for which patents are difficult to enforce and any other elements of our product candidate discovery and development processes that involve proprietary know-how, information or technology that is not covered by patents. 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, but it is possible that these security measures could be breached. Although we expect all of our employees and consultants to assign their inventions to us, and all of our employees, consultants, advisors and any third parties who have access to our proprietary know-how, information or technology to enter into confidentiality agreements, we cannot provide any assurances that all such agreements have been duly executed or 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. For example, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Misappropriation or unauthorized disclosure of our trade secrets could impair our competitive position and may have a material adverse effect on our business. Additionally, if the steps we take to maintain the confidentiality of our trade secrets are inadequate, we may have insufficient recourse against third parties for misappropriating our proprietary information and processes. In addition, others may independently discover our trade secrets and proprietary information. For example, the FDA, as part of its Transparency Initiative, is currently considering whether to make additional information publicly available on a routine basis, including information that we may consider to be trade secrets or other proprietary information, and it is not clear at the present time how the FDA's disclosure policies may change in the future, if at all.

If we are unable to prevent material disclosure of the non-patented intellectual property related to our technologies to third parties, and there is no guarantee that we will have any such enforceable trade secret protection, we may 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.

Further, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant problems in preventing third parties from practicing our inventions in countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions.

Claims that our product candidates or the manufacture, sale or use of our future products infringe the patent or other intellectual property rights of third parties could result in costly litigation or could require substantial time and money to resolve, even if litigation is avoided.

Our commercial success depends in part on our avoiding infringement of the patents and proprietary rights of third parties. There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, oppositions and inter partes reexamination proceedings before the United States Patent and Trademark Office, or USPTO, and corresponding foreign patent offices. 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 pursuing development candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the patent rights of third parties.

Third parties may assert that we are employing their proprietary technology without authorization. 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. Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that our product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes 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 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.

Similarly, if any third-party patents are held by a court of competent jurisdiction to cover aspects of our formulations, processes for manufacture or methods of use, the holders of any such patents may be able to block our ability to develop and commercialize the applicable product candidate unless we obtain a license or until such patent expires. In either case, such a license may not be available on commercially reasonable terms or at all.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further 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. 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, pay royalties, redesign our infringing products or obtain one or more licenses from third parties, which may not be able to be obtained on reasonable commercial terms or at all, or require substantial time and monetary expenditure.

We may not be successful in obtaining or maintaining necessary rights to our Physiocrine therapeutic product candidates and processes for our development pipeline through acquisitions and in-licenses.

We believe that we have rights to intellectual property, through licenses from third parties and under patents that we own, that is necessary or useful to develop our product candidates. Because our programs may involve additional product candidates that may require the use of proprietary rights held by third parties, the growth of our business will likely depend in part on our ability to acquire, in-license or use these proprietary rights. In addition, our product candidates may require specific formulations to work effectively and efficiently and these rights may be held by others. We may be unable to acquire or in-license any compositions, methods of use, processes or other third-party intellectual property rights from third parties that we identify on reasonable commercial terms or at all. 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, cash resources and greater clinical development and commercialization capabilities.

We sometimes collaborate with U.S. and foreign academic institutions to accelerate our preclinical research or development under written agreements with these institutions. These institutions may provide us with an option to negotiate a license to the institution's rights in technology resulting from the collaboration. Regardless of any such right of first negotiation for intellectual property, we may be unable to negotiate a license within the specified time frame or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to other parties, potentially blocking our ability to pursue our program.

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. If we are unable to successfully obtain rights to required third-party intellectual property rights, our business, financial condition and prospects for growth could suffer.

If we fail to comply with our obligations in the agreements under which we license intellectual property rights from third parties or otherwise experience disruptions to our business relationships with our licensors, we could lose license rights that are important to our business.

We are a party to a number of intellectual property license agreements that are important to our business and expect to enter into additional license agreements in the future. Our existing license agreements impose, and we expect that future license agreements will impose, various diligence, milestone payment, royalty and other obligations on us. If we fail to comply with our obligations under these agreements, or we are subject to a bankruptcy, the licensor may have the right to terminate the license, in which event we would not be able to market products covered by the license. For example, under the terms of the license agreements that we may enter into pursuant to our amended and restated research funding and option agreement with The Scripps Research Institute, or TSRI, TSRI has the right to terminate the license under various circumstances, including our failure to make payments to TSRI when due, our default in our indemnification and insurance obligations under the agreement, our failure to meet diligence obligations, as determined by TSRI, our underreporting or underpayment of amounts due to TSRI, our conviction of a felony related to the manufacture, use or sale of licensed products, services or processes and our institution of any challenges to the validity or enforceability of any of the licensed patents.

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 commercial terms, if at all. In that event, we may be required to expend significant time and resources to develop or license replacement technology. If we are unable to do so, we may be unable to develop or commercialize the affected product candidates, which could harm our business significantly. We cannot provide any assurances that third-party patents do not exist which might be enforced against our current product candidates or future products, resulting in either an injunction prohibiting our sales, or, with respect to our sales, an obligation on our part to pay royalties or other forms of compensation to third parties.

In some cases, patent prosecution of our licensed technology is controlled by the licensor. Under the license agreements that we may enter into pursuant to our amended and restated research funding and option agreement with TSRI, TSRI is responsible for the prosecution and maintenance of the licensed patent rights, subject to our right to be consulted and to be informed of the progress of patent applications, patents and related submissions. If our licensors fail to obtain and maintain patent or other protection for the proprietary intellectual property we license from them, we could lose our rights to the intellectual property or our exclusivity with respect to those rights, and our competitors could market competing products using such intellectual property. In certain cases, we may control the prosecution of patents resulting from licensed technology. In the event we breach any of our obligations related to such prosecution, we may incur significant liability to our licensors. Licensing of intellectual property is of critical importance to our business and involves complex legal, business and scientific issues and is complicated by the rapid pace of scientific discovery in our industry. Disputes may arise regarding intellectual property subject to a license agreement, including:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the license agreement;
- the sublicensing of patent and other rights under our collaborative development relationships;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our sublicensees or partners, if any; and
- the priority of invention of patented technology.

If disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates.

We may become involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time-consuming and unsuccessful.

Competitors may infringe or otherwise violate our patents, the patents of our licensors or our other intellectual property rights. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. Any claims that we assert against perceived infringers could also provoke these parties to assert counterclaims against us alleging that we infringe their intellectual property rights. In addition, in an infringement proceeding, a court may decide that a patent of ours or our licensors is not valid, is unenforceable or is not infringed, or may refuse to stop the other party 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 or interpreted narrowly and could put our patent applications at risk of not issuing.

Interference or derivation proceedings provoked by third parties or brought by us may be necessary to determine the priority of inventions or other matters of inventorship with respect to our patents or patent applications or those of our licensors. We may also become involved in other proceedings, such as re-examination or opposition proceedings, before the USPTO or its foreign counterparts relating to our intellectual property or the intellectual property rights of others. An unfavorable outcome in any such proceedings could require us to cease using the related technology or to attempt to license rights to it from the prevailing party, or could cause us to lose valuable intellectual property rights. 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, alone or with our licensors, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States. In addition, the uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, continue our research programs, license necessary technology from third parties, or enter into development partnerships that would help us bring our product candidates to market. We may also become involved in disputes with others regarding the ownership of intellectual property rights. For example, we jointly develop intellectual property with certain parties, and disagreements may therefore arise as to the ownership of the intellectual property developed pursuant to these relationships. If we are unable to resolve these disputes, we could lose valuable intellectual property rights.

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. There could also 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 material adverse effect on the price of our common stock.

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 their former employers.

We employ individuals who were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants and independent contractors 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 our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of any of our employee's former employer or other third parties. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, which could adversely impact our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property.

We may be subject to claims that former employees, collaborators or other third parties have an ownership interest in our patents or other intellectual property. For example, we may have inventorship disputes arise from conflicting obligations of consultants or others who are involved in developing our product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership, or we may enter into agreements to clarify the scope of our rights in such intellectual property. 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.

Obtaining and maintaining our 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.

Periodic maintenance fees, renewal fees, annuity fees and various other governmental fees on patents or applications will be due to be paid to the USPTO and various governmental patent agencies outside of the United States in several stages over the lifetime of the patents or applications. We have systems in place to remind us to pay these fees, and we employ an outside firm and rely on our outside counsel to pay these fees due to non-U.S. patent agencies. The USPTO 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. We employ law firms and other professionals to help us comply, and 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 non-compliance 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.

Issued patents covering our product candidates could be found invalid or unenforceable if challenged in court.

If we or one of our licensors initiated legal proceedings against a third party to enforce a patent covering one of our product candidates, the defendant could counterclaim that the patent covering our product candidate is invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, 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, post grant review, and equivalent proceedings in foreign jurisdictions (e.g., opposition proceedings). Such proceedings could result in revocation or amendment to our patents in such a way that they no longer cover our product candidates. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art, of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity 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 would have a material adverse impact on our business.

Changes in patent law could diminish the value of patents in general, thereby impairing our ability to protect our products.

As is the case with many other biotechnology companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biotechnology industry involve both technological and legal complexity, and therefore obtaining, maintaining and enforcing biotechnology patents is costly, time-consuming and inherently uncertain. In addition, recent legislative and judicial developments in the United States and elsewhere have in some cases removed the protection afforded to patent owners, made patents more difficult to obtain, or increased the uncertainty regarding the ability to obtain, maintain and enforce patents. For example, Congress has recently passed, and the United States is currently implementing, wide-ranging patent reform legislation, and may pass further patent reform legislation in the future. 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. For example, in a recent case, *Association for Molecular Pathology v. Myriad Genetics, Inc.*, the U.S. Supreme Court held that certain claims to naturally occurring substances are not patentable. Although we do not believe that any of the patents owned or licensed by us will be found invalid based on this decision, we cannot predict how future decisions by the courts, the U.S. Congress, or the USPTO may impact the value of our patents. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents generally, once obtained. Depending on decisions and actions by the U.S. Congress, the federal courts, the USPTO and their respective foreign counterparts, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to maintain and enforce our existing patents and patents that we might obtain in the future.

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

On September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes a number of significant changes to U.S. patent law, including provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. The USPTO 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, were enacted March 16, 2013. Although it is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business, 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.

We have not yet registered Resolaris or Stalaris as a trademark, and failure to secure or maintain adequate protection for our trademarks could adversely affect our business.

We have filed U.S. trademark applications for the Resolaris and Stalaris marks but they have not yet matured to registration, and we have yet to file any foreign trademark applications for the Resolaris or Stalaris marks. The USPTO has examined our U.S. application for the Resolaris mark and there are no outstanding objections to the application. The USPTO has yet to begin the examination process for our application to register the Stalaris mark, and it could raise objections to our application. Although we would be given an opportunity to respond to those objections, we may be unable to overcome such objections. In addition, in the USPTO 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 have been filed and may in the future be filed against certain of our trademark applications or registrations, and our trademark applications or registrations may not survive such proceedings. Furthermore, third parties have alleged, and may allege in the future, that the Resolaris or Stalaris marks in particular or any other trademark or trade name that we elect to use for our product candidates, may cause confusion in the marketplace. Specifically, in April 2015, Alexion Pharmaceuticals (Alexion) sent a letter to our counsel alleging that our anticipated use of the Resolaris trademark would cause patients, practitioners and researchers to mistakenly associate us with Alexion or its Soliris product. Alexion claims ownership of a U.S. trademark registration for its Soliris mark. Alexion concluded its letter by requesting that we select a new name for our Resolaris product and withdraw our pending trademark application for the mark. In February 2017 our counsel received a letter from counsel to Novartis AG (Novartis) alleging that our anticipated use of the Stalaris trademark would cause consumer confusion with its Ilaris product. Novartis claims ownership of a U.S. trademark registration for its Ilaris mark. Additionally, Novartis also expressed concerns about the potential for confusion between the Resolaris mark and Novartis' Ilaris mark. Novartis concluded its letter by demanding that we abandon our U.S. trademark application for the Stalaris mark. We evaluate such actual and potential allegations in the course of our business, and such evaluations may cause us to change our commercialization or branding strategy for our product candidates, which may require us to incur additional costs. In particular, we are assessing Alexion and Novartis' allegations and will determine whether we need to, or should, select a different name for the product or contest any trademark enforcement actions. 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 able to protect our intellectual property rights throughout the world.

Filing, prosecuting and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. 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 that in the United States. These products may compete with our products and our patents or other intellectual property rights may not be effective or sufficient to prevent them from 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, trade secrets and other intellectual property protection, particularly those relating to biotechnology products, 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 costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Risks related to our business operations

Our future success depends on our ability to retain key employees, consultants and advisors and to attract, retain and motivate qualified personnel.

We are highly dependent on principal members of our executive team, the loss of whose services may adversely impact the achievement of our objectives. While we have entered into employment agreements with each of our executive officers, any of them could leave our employment at any time, as all of our employees are "at will" employees. Recruiting and retaining other qualified employees, consultants and advisors for our business, including scientific and technical personnel, will also be critical to our success. There is currently a shortage of skilled personnel in our industry, which is likely to continue. As a result, competition for skilled personnel is intense and the turnover rate can be high. We may not be able to attract and retain personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for individuals with similar skill sets. In addition, the available pool of skilled employees may be further reduced if immigration laws change in a manner that increases restrictions on immigration. Failure to succeed in preclinical studies or clinical trials may make it more challenging to recruit and retain qualified personnel. The inability to recruit or loss of the services of any executive, key employee, consultant or advisor may impede the progress of our research, development and commercialization objectives. Furthermore, our common stock is currently trading at a price below the exercise price of most of our outstanding stock options. As a result, these "under water" options are less useful as a motivation and retention tool for our existing employees. Conversely, if our employees exercise outstanding stock options and sell their stock in the public market resulting in significant gains, we may experience an increased turnover rate.

We are subject to a variety of risks associated with international operations that could materially adversely affect our business.

We currently conduct research activities through our majority-owned (98%) Hong Kong subsidiary, Pangu BioPharma Limited, in collaboration with the Hong Kong University of Science and Technology. Additionally, we are currently conducting our Phase 1b/2 clinical trials of Resolaris in patients with FSHD and LGMD2B in the European Union. If any of our product candidates are approved for commercialization outside of the United States, we expect to either use our own sales organization or selectively enter into agreements with third parties to market our products on a worldwide basis or in more limited geographical regions. We are, and we expect that we will continue to be, subject to a variety of risks related to international operations, including:

- different regulatory requirements for approval of drugs and biologics in foreign countries;
- reduced or uncertain protection for intellectual property;
- unexpected changes in tariffs, trade barriers and regulatory requirements;
- economic weakness, including inflation, or political instability in particular foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad; and
- foreign currency fluctuations, which could result in reduced revenues, and other obligations incident to doing business in another country.

Any failure to continue our international operations or to commercialize our product candidates outside of the United States may impair our ability to generate revenues and harm our business, prospects and results of operations.

We may need to expand our organization and we may experience difficulties in managing this growth, which could disrupt our operations.

As we continue our ongoing Phase 1b/2 clinical trials of Resolaris, prepare for additional clinical trials of Resolaris and Stalaris and expand our other clinical development activities, as well as continue our operations as a public company, we may increase our full-time employee base and hire more consultants and contractors. In addition to certain members of our management team being relatively new to our company, our management may need to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing these growth activities. We may not be able to effectively manage the expansion of our operations, which may result in weaknesses in our infrastructure, operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Our expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the conduct of additional clinical activities for Resolaris and the development of additional product candidates. If our management is unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate or grow revenues could be reduced, and we may not be able to implement our business strategy. Our future financial performance and our ability to develop and commercialize product candidates and compete effectively will depend, in part, on our ability to effectively manage any future growth.

We may use our financial and human resources to pursue a particular business strategy, research program or product candidate and fail to capitalize on strategies, programs or product candidates that may be more profitable or for which there is a greater likelihood of success.

Because we have limited resources, we may forego or delay pursuit of certain strategic opportunities or opportunities with certain programs or product candidates or for 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. In addition, we may elect to pursue a research, clinical or commercial strategy that ultimately does not yield the results that we desire. Our spending on current and future research and development programs for product candidates may not result in 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 strategic collaboration, 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, or we may allocate internal resources to a product candidate in a therapeutic area or market in which it would have been more advantageous to enter into a partnering arrangement. Any failure to allocate resources or capitalize on strategies in a successful manner will have an adverse impact on our business.

Our employees, principal investigators, consultants and commercial partners may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading.

We are exposed to the risk of fraud or other misconduct by our employees, principal investigators, consultants and commercial partners. Misconduct by these parties could include intentional failures to comply with the regulations of the FDA and non-U.S. regulators, provide accurate information to the FDA and non-U.S. regulators, comply with healthcare fraud and abuse laws and regulations in the United States and abroad, report financial information or data accurately or disclose unauthorized activities to us. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Such misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and cause serious harm to our reputation. We have adopted a code of conduct applicable to all of our employees, but it is not always possible to identify and deter employee misconduct, 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 comply with these laws or regulations. 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, including the imposition of significant fines or other sanctions.

We face potential product liability, and, if successful claims are brought against us, we may incur substantial liability and costs. If the use of our product candidates harms patients, or is perceived to harm patients even when such harm is unrelated to our product candidates, our regulatory approvals could be revoked or otherwise negatively impacted and we could be subject to costly and damaging product liability claims.

The use of our product candidates in clinical trials and the sale of any products for which we obtain marketing approval exposes us to the risk of product liability claims. Product liability claims might be brought against us by patients, healthcare providers, pharmaceutical companies or others selling or otherwise coming into contact with our products. There is a risk that our product candidates may induce adverse events. If we cannot successfully defend against product liability claims, we could incur substantial liability and costs. In addition, regardless of merit or eventual outcome, product liability claims may result in:

- impairment of our business reputation;
- withdrawal of clinical trial participants;
- costs due to related litigation;
- distraction of management's attention from our primary business;
- substantial monetary awards to patients or other claimants;
- the inability to commercialize our product candidates; and
- decreased demand for our product candidates, if approved for commercial sale.

We carry product liability insurance for our clinical trials covering $5.0 million per occurrence and up to $5.0 million in the aggregate, subject to certain deductibles and exclusions. Although we believe the amount of our insurance coverage is typical for companies similar to us in our industry, we may not have adequate insurance coverage or be able to maintain insurance coverage at a reasonable cost or in sufficient amounts to protect us against losses due to liability. If and when we obtain marketing approval for product candidates, we intend to expand our insurance coverage to include the sale of commercial products; however, we may be unable to obtain product liability insurance on commercially reasonable terms or in adequate amounts. On occasion, large judgments have been awarded in class action lawsuits based on drugs or medical treatments that had unanticipated adverse effects. A successful product liability claim or series of claims brought against us could cause our stock price to decline and adversely affect our reputation and, if judgments exceed our insurance coverage, could adversely affect our results of operations and business.

Patients with the diseases targeted by our product candidates are often already in severe and advanced stages of disease and may have both known and unknown significant pre-existing and potentially life-threatening health risks. During the course of treatment, patients may suffer adverse events, including death, for reasons that may be related to our product candidates. Such events could subject us to costly litigation, require us to pay substantial amounts of money to injured patients, delay, negatively impact or end our opportunity to receive or maintain regulatory approval to market our products, or require us to suspend or abandon our commercialization efforts. Even in a circumstance in which we do not believe that an adverse event is related to our products, the investigation into the circumstance may be time-consuming or inconclusive. These investigations may interrupt our sales efforts, delay our regulatory approval process in other countries, or impact and limit the type of regulatory approvals our product candidates receive or maintain. As a result of these factors, a product liability claim, even if successfully defended, could have a material adverse effect on our business, financial condition or 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.

We are subject to anti-corruption laws in the jurisdictions in which we operate.

We are subject to a number of anti-corruption laws, including the U.S. Foreign Corrupt Practices Act, or the FCPA, and various other anti-corruption laws. The FCPA generally prohibits companies and their intermediaries from making improper payments to foreign officials for the purpose of obtaining or keeping business and/or other benefits. Our business relies on approvals and licenses from government and regulatory entities, and as a result, we are subject to certain elevated risks associated with interactions with these entities. Although we have adopted a code of business conduct and ethics that includes provisions governing the interactions of employees with government entities to mitigate these risks. If we are not in compliance with anti-corruption laws and other laws governing the conduct of business with government entities (including local laws), we may be subject to criminal and civil penalties and other remedial measures, which could harm our reputation and have a material adverse impact on our business, financial condition, results of operations and prospects. Any investigation of any actual or alleged violations of such laws could also harm our reputation or have an adverse impact on our business, prospects, financial condition and results of operations.

We will incur significant increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives.

As a public company, we will incur significant legal, accounting and other expenses that we did not incur as a private company. In addition, the Sarbanes-Oxley Act of 2002, or Sarbanes-Oxley Act, as well as rules subsequently implemented by the Securities and Exchange Commission, or SEC, and The Nasdaq Global Select Market have imposed various requirements on public companies. In July 2010, the Dodd-Frank Wall Street Reform and Consumer Protection Act, or the Dodd-Frank Act, was enacted. There are significant corporate governance and executive compensation related provisions in the Dodd-Frank Act that require the SEC to adopt additional rules and regulations in these areas such as "say on pay" and proxy access. Recent legislation permits smaller "emerging growth companies" to implement many of these requirements over a longer period and up to five years from the pricing of our IPO. We have elected to take advantage of this legislation but cannot guarantee that we will not be required to implement these requirements sooner than budgeted or planned and thereby incur unexpected expenses. Stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate. Our management and other personnel will need to devote a substantial amount of time to these compliance initiatives. 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 these rules and regulations to make it more difficult and more expensive for us to maintain director and officer liability insurance and we have been required to incur substantial costs to maintain our current levels of such coverage.

Unfavorable global economic conditions could adversely affect our business, financial condition or results of operations.

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. The recent global financial crisis caused extreme volatility and disruptions in the capital and credit markets. For example, in the recent U.K. referendum on its membership in the European Union resulted in a vote in favor of leaving the European Union (commonly referred to as "Brexit"), which could lead to a period of considerable uncertainty, particularly in relation to global financial markets which in turn could adversely affect our ability to raise additional capital. A severe or prolonged economic downturn, such as the recent global financial crisis, could result in a variety of risks to our business, including inability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could also strain our manufacturers, possibly resulting in supply disruption. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

We or the third parties upon whom we depend may be adversely affected by earthquakes, droughts, floods, fires or other natural disasters and our business continuity and disaster recovery plans may not adequately protect us from a serious disaster.

We are located in San Diego, California and our manufacturing activities are conducted by contract manufacturing organizations at various locations in the United States. We currently anticipate that if Resolaris receives marketing approval, commercial production may take place in the United States and/or the United Kingdom. Some of these geographic locations have in the past experienced natural disasters, including severe earthquakes. Earthquakes, droughts, floods, fires, disease epidemics 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 facilities, that damaged critical infrastructure, such as the manufacturing facilities of our third-party contract manufacturers, 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. The disaster recovery and business continuity plans we have in place currently are limited and are unlikely to prove adequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, as well as limits on our insurance coverage, which could have a material adverse effect on our business, prospects, financial condition and results of operations.

Risks related to the ownership of our common stock

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

The market price of our common stock is likely to be volatile. Our stock price could be subject to wide fluctuations in response to a variety of factors, including the following:

- adverse results or delays in preclinical studies or clinical trials;
- the imposition of a clinical hold on our product candidates or our inability to cause the clinical hold to be lifted;
- any delay in filing a BLA, NDA or IND for any of our product candidates and any adverse development or perceived adverse development with respect to the FDA's review of that BLA, NDA or IND;
- failure to successfully develop and commercialize our product candidates;
- the perception of limited market sizes or pricing for our product candidates;
- failure by us or our licensors to prosecute, maintain or enforce intellectual property rights covering our product candidates and processes;
- changes in laws or regulations applicable to future products;
- inability to obtain adequate product supply for our product candidates or the inability to do so at acceptable prices;
- adverse regulatory decisions;
- introduction of new products, services or technologies by our competitors;
- inability to obtain additional capital;
- failure to meet or exceed financial or operational projections we may provide to the public;
- failure to meet or exceed the financial or operational projections of the investment community;
- the perception of the pharmaceutical industry by the public, politicians, legislatures, regulators and the investment community;
- significant acquisitions, strategic partnerships, joint ventures or capital commitments by us or our competitors;

- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- additions or departures of key scientific or management personnel;
- significant lawsuits, including patent or stockholder litigation;
- if securities or industry analysts do not publish research or reports about our business, or they issue an adverse or misleading opinion regarding our stock;
- changes in the market valuations of similar companies;
- general market or macroeconomic conditions;
- sales of our common stock by us or our stockholders in the future; and
- trading volume of our common stock.

In addition, companies trading in the stock market in general, and The Nasdaq Global Select 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.

Our executive officers, directors, principal stockholders and their affiliates own a significant percentage of our stock and will be able to exert significant control over matters submitted to stockholders for approval.

As of March 8, 2017, based on the latest information publicly available to us, our executive officers, directors, five percent stockholders and their affiliates beneficially own approximately 69% of our voting stock. Therefore, these stockholders will have the ability to influence us through their ownership positions and may be able to determine all matters requiring stockholder approval. For example, these stockholders, acting together, 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 may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may believe are in your best interest as one of our stockholders.

We are an "emerging growth company," and we cannot be certain if the reduced reporting requirements applicable to emerging growth companies will make our common stock less attractive to investors.

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act reduced disclosure obligations regarding executive compensation and our periodic reports and proxy statements and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. We could be an emerging growth company for up to five years from the pricing of our IPO, although circumstances could cause us to lose that status earlier, including if the market value of our common stock held by non-affiliates exceeds $700 million as of any June 30 before that time or if we have total annual gross revenue of $1 billion or more during any fiscal year before that time, in which cases we would no longer be an emerging growth company as of the following December 31 or, if we issue more than $1 billion in non-convertible debt during any three-year period before that time, we would cease to be an emerging growth company immediately. Even after we no longer qualify as an emerging growth company, we may still qualify as a "smaller reporting company" which would allow us to take advantage of many of the same exemptions from disclosure requirements, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act and reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

Under the JOBS Act, emerging growth companies can also 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 from new or revised accounting standards and, therefore, will be subject to the same new or revised accounting standards as other public companies that are not emerging growth companies.

Future sales and issuances of equity or debt securities could result in dilution to our stockholders, impose restrictions or limitations on our business and could cause our stock price to fall.

We will need additional capital in the future to continue our planned operations, and we may seek additional funding through a combination of equity offerings, debt financings, government or other third-party funding and other collaborations, strategic alliances and licensing arrangements. These financing activities may have an adverse effect on our stockholders' rights, the market price of our common stock and on our operations, and may require us to relinquish rights to some of our technologies, intellectual property or product candidates, issue additional equity or debt securities, or otherwise agree to terms unfavorable to us. We have an effective shelf registration statement on Form S-3 that provides for the sale of up to $150 million in the aggregate of common stock, preferred stock, debt securities, warrants and/or units by us from time to time in one or more offerings. We have also entered into a sales agreement with Cowen and Company, LLC for the sale of up to $35 million of common stock, from time to time, $20 million of which is currently registered under the Form S-3. To date, no shares of common shares have been sold pursuant to such sales agreement. Any future debt financings may impose restrictive covenants or otherwise adversely affect the holdings or the rights of our stockholders, and any equity financings will be dilutive to our stockholders. Furthermore, additional equity or debt financing might not be available to us on reasonable terms, if at all.

In additional, sales of a substantial number of shares of our common stock by our existing stockholders 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. Certain holders of our securities are entitled to rights with respect to the registration of their shares under the Securities Act pursuant to a registration and voting rights agreement. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act. Any sales of securities by these stockholders could have a material adverse effect on the trading price of our common stock, even if there is no relationship between such sales and the performance of our business.

We have also registered all common stock that we may issue under our employee benefits plans. As a result, these shares can be freely sold in the public market upon issuance, subject to restrictions under the securities laws. In addition, our directors and executive officers may establish programmed selling plans under Rule 10b5-1 of the Securities Exchange Act for the purpose of effecting sales of our common stock. Further, we intend to file a registration statement on Form S-8 to register the shares of common stock underlying the option to purchase up to 145,000 shares of our common stock that has been granted as an inducement grant prior to the time at which such option becomes exercisable. If any of these events cause a large number of our shares to be sold in the public market, the sales could reduce the trading price of our common stock and impede our ability to raise future capital.

If securities analysts do not publish research or reports about our business or if they publish negative evaluations of our stock, the price of our stock could decline.

The trading market for our common stock will rely in part on the research and reports that industry or financial analysts publish about us or our business. We may never obtain research coverage by industry or financial analysts. If no or few analysts commence coverage of us, the trading price of our stock would likely decrease. Even if we do obtain analyst coverage, if one or more of the analysts covering our business downgrade their evaluations of our stock, the price of our stock could decline. If one or more of these analysts cease to cover our stock, we could lose visibility in the market for our stock, which in turn could cause our stock price to decline.

We could be subject to securities class action litigation.

In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because pharmaceutical companies have experienced significant stock 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.

We have broad discretion in the use of our cash and cash equivalents and may not use them effectively.

We have considerable discretion in the application of our existing cash and cash equivalents. We expect to use our existing cash to fund research and development activities and for working capital and general corporate purposes, including funding the costs of operating as a public company. In addition, pending their use, we may invest our existing cash in short-term, investment-grade, interest-bearing securities. We may use these proceeds for purposes that do not yield a significant return or any return at all for our stockholders.

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

We have incurred substantial losses during our history, we do not expect to become profitable in the near future and we may never achieve profitability. Unused losses generally are available to be carried forward to offset future taxable income, if any, until such unused losses expire. Under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, if a corporation undergoes an "ownership change," generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period, the corporation's ability to use its pre-change net operating loss carryforwards, or NOLs, and other pre-change tax attributes (such as research tax credits) to offset its post-change taxable income or taxes may be limited. We completed an analysis through September 7,

2011, and determined that on November 30, 2006 an ownership change occurred, for which we have adjusted our NOL and research and development tax credit carryforwards. We may have experienced an ownership change subsequent to September 7, 2011, including as a result of our IPO, and we may also experience ownership changes in the future as a result of subsequent shifts in our stock ownership, some of which may be outside of our control. As a result, our ability to use our pre-change NOLs to offset U.S. federal taxable income may be subject to limitations, which could potentially result in increased future tax liability to us. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed.

We do not intend to pay dividends on our common stock, and therefore any returns will be limited to the value of our stock.

We have never declared or paid any cash dividends on our common stock. We 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. Any return to stockholders will therefore be limited to the appreciation of their stock.

Provisions in our amended and restated certificate of incorporation and bylaws, as well as provisions of Delaware law, could make it more difficult for a third party to remove our current management, acquire us or increase the cost of acquiring us, even if doing so would benefit our stockholders.

Our amended and restated certificate of incorporation, amended and restated bylaws and Delaware law contain provisions that may have the effect of delaying or preventing a change in control of us or changes in our management. Our amended and restated certificate of incorporation and bylaws include provisions that:

- authorize "blank check" preferred stock, which could be issued by our board of directors without stockholder approval and may contain voting, liquidation, dividend and other rights superior to our common stock;
- create a classified board of directors whose members serve staggered three-year terms;
- specify that special meetings of our stockholders can be called only by our board of directors, the chairperson of our board of directors, our chief executive officer or our president;
- prohibit stockholder action by written consent;
- establish an advance notice procedure for stockholder approvals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to our board of directors;
- provide that our directors may be removed only for cause;
- provide that vacancies on our board of directors may be filled only by a majority of directors then in office, even though less than a quorum;
- specify that no stockholder is permitted to cumulate votes at any election of directors;
- expressly authorize our board of directors to modify, alter or repeal our amended and restated bylaws; and
- require supermajority votes of the holders of our common stock to amend specified provisions of our amended and restated certificate of incorporation and amended and restated bylaws.

These provisions, alone or together, could delay or prevent hostile takeovers and changes in control or changes in our management.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which limits the ability of stockholders owning in excess of 15% of our outstanding voting stock to merge or combine with us.

Any provision of our amended and restated certificate of incorporation or amended and restated bylaws or Delaware law that has the effect of delaying or deterring a change in control could limit the opportunity for our stockholders to receive a premium for their shares of our common stock, and could also affect the price that some investors are willing to pay for our common stock.

Item 1B. Unresolved Staff Comments

Not applicable.

Item 2. Properties

Our administrative offices and research laboratory are located in San Diego, California. We lease approximately 17,083 square feet of office and laboratory space (Primary Facility) under an operating lease that expires in May 2017 and 7,411 square feet (Additional Space) we subleased with a tenant of our landlord that expires in June 2017. In January 2017, we extended our Primary Facility lease with our landlord through May 2019 for an additional commitment of $1.5 million and we have an option with our landlord to include the Additional Space within our lease through May 2019. We believe that our facility is sufficient to meet our needs and that suitable additional space will be available as and when needed.

Item 3. Legal Proceedings

We are not a party to any material legal proceedings at this time. From time to time, we may be subject to various legal proceedings and claims that arise in the ordinary course of our business activities. Although the results of litigation and claims cannot be predicted with certainty, we do not believe we are party to any claim or litigation the outcome of which, if determined adversely to us, would individually or in the aggregate be reasonably expected to have a material adverse effect on our results of operations or financial condition. Regardless of the outcome, litigation can have an adverse effect on us because of defense and settlement costs, diversion of management resources and other factors.

Item 4. Mine Safety Disclosure

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 Select Market on May 7, 2015 and trades under the symbol "LIFE". Prior to such time, there was no public market for our common stock. The following table sets forth the high and low sales prices per share of our common stock for the periods indicated as reported on The NASDAQ Global Select Market.

	Price Range	
	High	Low
Year Ended December 31, 2016:		
First Quarter	$ 9.63	$ 3.50
Second Quarter	$ 4.36	$ 2.48
Third Quarter	$ 3.85	$ 2.62
Fourth Quarter	$ 3.80	$ 2.10

	Price Range	
	High	Low
Year Ended December 31, 2015:		
Second Quarter (commencing May 6, 2015)	$ 28.29	$ 12.90
Third Quarter	$ 21.00	$ 9.59
Fourth Quarter	$ 13.26	$ 7.37

Holders of Record

As of March 8, 2017, there were approximately 68 holders of record of our common stock. The approximate number of holders is based upon the actual number of holders registered in our records at such date and excludes holders in "street name" or persons, partnerships, associations, corporations, or other entities identified in security positions listings maintained by depository trust companies.

Dividend Policy

We have never declared or paid any cash dividends on our common stock. We currently intend to retain all available funds and any future earnings to support our operations and finance the growth and development of our business. We do not intend to pay cash dividends on our common stock for the foreseeable future. Any future determination related to our dividend policy will be made at the discretion of our board of directors and will depend upon, among other factors, our results of operations, financial condition, capital requirements, contractual restrictions, business prospects and other factors our board of directors may deem relevant.

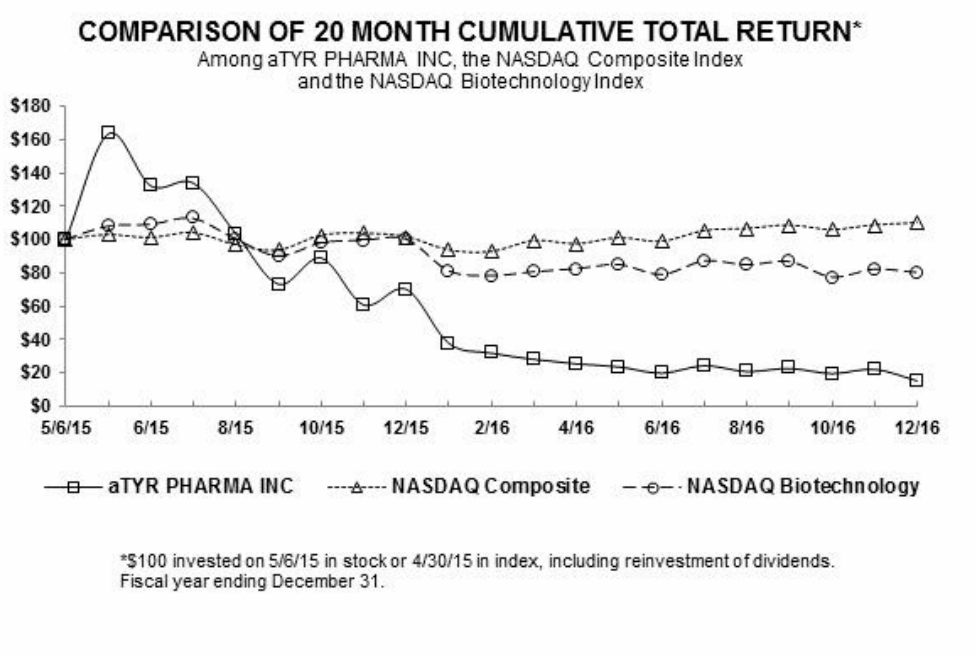
Securities Authorized for Issuance Under Equity Compensation Plans

Information about our equity compensation plans is incorporated herein by reference to Item 12 of Part III of this Annual Report.

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 following graph shows a comparison from May 7, 2015 (the date our common stock commenced trading on The NASDAQ Global Select Market) through December 31, 2016 of the cumulative total return for our common stock, the NASDAQ Biotechnology Index (NBI) and the NASDAQ Composite Index (CCMP). The graph assumes an initial investment of $100 on May 7, 2015. The comparisons in the graph are not intended to forecast or be indicative of possible future performance of our common stock



Recent Sales of Unregistered Securities

During the year ended December 31, 2016, we did not issue or sell any unregistered securities not previously disclosed in a Quarterly Report on Form 10-Q or in a Current Report on Form 8-K.

Issuer Purchases of Equity Securities

We did not repurchase any securities during the quarter ended December 31, 2016.

Item 6. Selected Financial Data.

The selected financial data set forth below is derived from our audited consolidated financial statements and may not be indicative of future operating results. The following selected financial data should be read in conjunction with the Consolidated Financial Statements and notes thereto and Item 7, "Management's Discussion and Analysis of Financial Condition and Results of Operations" included elsewhere in this Annual Report on Form 10-K. Amounts are in thousands, except per share amounts.

	Years Ended December 31,		
	2016	2015	2014
Statements of Operations Data:			
Loss from operations	$ (57,940)	$ (47,616)	$ (23,554)
Net loss	(57,855)	(47,973)	(24,350)
Comprehensive loss	(57,760)	(48,144)	(24,350)
Net loss per share, basic and diluted	$ (2.44)	$ (3.03)	$ (29.69)
Weighted average shares outstanding, basic and diluted	23,681,019	15,838,353	834,221

	As of December 31,		
	2016	2015	2014
Consolidated Balance Sheet Data:			
Cash, cash equivalents and available-for-sale investments	$ 76,149	$ 125,349	$ 15,853
Total assets	80,524	129,675	20,644
Preferred stock warrant liabilities	—	—	319
Convertible promissory note	—	—	2,000
Working capital	66,243	85,802	6,396
Long-term debt, net of current portion and issuance costs	9,198	1,776	5,142
Redeemable convertible preferred stock	—	—	95,619
Accumulated deficit	(215,979)	(158,124)	(110,151)
Total stockholders' deficit	62,801	115,050	(91,010)

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

You should read the following discussion and analysis together with "Item 6. Selected Financial Data" and the consolidated financial statements and related notes included elsewhere in this Annual Report on Form 10-K. The following discussion contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those expressed or implied in any forward-looking statements as a result of various factors, including those set forth under the caption "Item 1A. Risk Factors."

Overview

We engage in the discovery and clinical development of innovative medicines for patients suffering from severe, rare diseases using our knowledge of Physiocrine biology, a newly discovered set of physiological pathways. Through our research efforts, we believe that Physiocrines evolved over billions of years to promote homeostasis in complex organisms. We have evidence to support that some of these proteins evolved to govern and orchestrate the mammalian immune system. We believe immune imbalance is underappreciated in many disease types and may ultimately be responsible for much of the pathophysiology associated with a number of important genetic and immunology based diseases.

By focusing on immune pathways in disease, we believe our therapeutic candidates have the potential to restore patients to a healthier state, achieve homeostatic balance and ultimately lead to improved clinical outcomes. To date, our discovery efforts have generated three immunology-based investigational innovative therapeutic programs in three different therapeutic areas:

- **Resolaris**: We internally discovered and developed Resolaris, our first Physiocrine-based therapeutic candidate, based on a protein naturally secreted from muscle that acts on T-cells at the tissue level to promote healthier muscle. We believe this may translate into an innovative therapeutic for rare genetic myopathies with an immune component (e.g. T-cells in the patients' muscle), including limb-girdle muscular dystrophy (LGMD), facioscapulohumeral muscular dystrophy (FSHD), and Duchenne muscular dystrophy (DMD). Resolaris also represents an example of our first therapeutic modality - natural protein therapy – adding back a pathway that is insufficiently produced by the human body to counteract disease.
- **Stalaris:** Our scientists successfully engineered the first fusion protein with a Physiocrine, Stalaris, to provide designed properties to enhance the immuno-modulatory aspects of a Physiocrine *in vivo*. We plan to develop Stalaris as a potential therapeutic for patients with rare pulmonary diseases with an immune component, including interstitial lung disease. This fusion protein, which utilizes the Fc region of an antibody, also potentially represents a novel Fc-Physiocrine platform for future Physiocrine-based therapies.
- **Project ORCA:** Our third program, represents a third therapeutic modality distinct from Resolaris or Stalaris. It also diversifies our pipeline by addressing severe diseases in a therapeutic area that differs from those of our first two programs. We use code name "Project ORCA" for this preclinical research program.

Our expansive Physiocrine patent estate provides us with potential product protection as we pioneer this new and important area of human biology. To protect our industry unique pipeline based on our proprietary new biology, we have built an intellectual property estate comprising over 175 issued patents or allowed patent applications that are owned or exclusively licensed by us, including over 300 potential Physiocrine-based protein compositions. We believe it is in the best interest of our stakeholders, including patients, caregivers, and our stockholders, to advance one or more of our three current programs based on Physiocrine biology with the expertise of or funding from appropriate strategic partners.

Since our inception in 2005, we have devoted substantially all of our resources to the therapeutic application of Physiocrines, including the preclinical development of and clinical trials for Resolaris, the creation, licensing and protection of related intellectual property and the provision of general and administrative support for these operations. We have not generated any revenue from product sales and, through December 31, 2016, have funded our operations primarily with the aggregate proceeds from the sales of our common stock in our initial public offering (IPO), private placement of redeemable convertible preferred stock and convertible promissory notes, commercial bank debt and a convertible promissory note issued to our landlord.

In May 2015, we completed our IPO whereby we sold 6,164,000 shares of common stock at a public offering price of $14.00 per share. As a result of the IPO, we raised a total of $75.9 million in net proceeds after deducting underwriting discounts and commissions of approximately $6.0 million and offering expenses of approximately $4.4 million. In addition, in connection with the IPO, all outstanding redeemable convertible preferred stock converted into 16,279,859 shares of our common stock.

In June 2016, we filed a Registration Statement on Form S-3 (File No. 333-211998) containing two prospectuses: (i) a base prospectus which covers the offering, issuance and sale of up to $150.0 million in the aggregate of an indeterminate number of shares of common stock and preferred stock, an indeterminate principal amount of debt securities and an indeterminate number of warrants and units; and (ii) a sales agreement prospectus covering the offering, issuance and sale of up to a maximum aggregate offering price of $20.0 million of our common stock that may be sold from time to time under a sales agreement with Cowen and Company, LLC (Cowen). In accordance with the terms of such sales agreement entered with Cowen, we may offer and sell shares of our common stock having an aggregate offering price of up to $35.0 million from time to time through Cowen. To date, no shares of common stock have been sold pursuant to such sales agreement. We will be required to file another prospectus supplement in the event we intend to offer more than $20.0 million in shares of our common stock in accordance with the sales agreement. The sales agreement prospectus amount of $20.0 million is included in the base prospectus amount of $150.0 million.

We have never been profitable and have incurred net losses in each annual and quarterly period since our inception. For the years ended December 31, 2016, 2015 and 2014, we have incurred consolidated net losses of $57.9 million, $48.0 million and $24.4 million, respectively. As of December 31, 2016, we had an accumulated deficit of $216.0 million.

Substantially all of our net losses resulted from costs incurred in connection with our development of and clinical trials for Resolaris, our other research and development programs and from general and administrative costs associated with our operations. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future, at least until we apply for and receive regulatory approval for Resolaris, Stalaris or another product candidate and generate substantial revenues from its commercialization, if ever. Our net losses may fluctuate significantly from quarter to quarter and year to year, depending on the nature and extent of our research and development expenses and clinical trials. We expect our expenses will increase substantially in connection with our ongoing activities as we:

- conduct clinical trials of Resolaris, Stalaris and any additional product candidates we may develop;
- continue our research and product development efforts;
- manufacture preclinical study and clinical trial materials;
- expand, protect and maintain our intellectual property portfolio;
- seek regulatory approvals for our product candidates that successfully complete clinical trials;
- hire additional staff, including clinical, operational, financial and technical personnel, if and when necessary, to execute on our business plan and create additional infrastructure to support our operations as a public company; and
- implement operational, financial and management systems.

We do not expect to generate any revenues from product sales unless and until we successfully complete development and obtain regulatory approval for one or more of our product candidates, which we expect will take a number of years at a minimum. If we obtain regulatory approval for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. Accordingly, we will need to raise substantial additional capital beyond the net proceeds from our IPO. The amount and timing of our future funding requirements will depend on many factors, including the pace and results of our preclinical and clinical development efforts and the timing and nature of the regulatory approval process for our product candidates. We anticipate that we will seek to fund our operations through public or private equity or debt financings, collaborations, strategic partnerships or other sources. However, we may be unable to raise additional capital or enter into such other arrangements when needed on favorable terms or at all. Our failure to raise capital or enter into such other arrangements when needed would have a negative impact on our financial condition and ability to develop our product candidates.

Financial Operations Overview

Organization and Business; Principles of Consolidation

We conduct substantially all of our activities through aTyr Pharma, Inc., a Delaware corporation, at our facility in San Diego, California. aTyr Pharma, Inc. was incorporated in the state of Delaware in September 2005. The consolidated financial statements include the accounts of aTyr Pharma, Inc., and its 98% majority-owned subsidiary in Hong Kong, Pangu BioPharma Limited as of December 31, 2016. All intercompany transactions and balances are eliminated in consolidation.

Research and Development Expenses

To date, our research and development expenses have related primarily to the development of and clinical trials for Resolaris and to research efforts targeting the potential therapeutic application of other Physiocrine-based immuno-modulators in rare disease indications. These expenses consist primarily of:

- salaries and employee-related expenses, including stock-based compensation and benefits for personnel in research and product development functions;
- costs associated with conducting our preclinical, development and regulatory activities, including fees paid to third-party professional consultants, service providers and our scientific, therapeutic and clinical advisory board;
- costs to acquire, develop and manufacture preclinical study and clinical trial materials;
- costs incurred under clinical trial agreements with clinical research organizations, or CROs, and investigative sites;
- costs for laboratory supplies;
- payments and stock issuances related to licensed products and technologies; and
- allocated facilities, depreciation and other allocable expenses.

Research and development costs are expensed as incurred. Clinical trial and other development costs incurred by third parties are expensed as the contracted work is performed. We accrue for costs incurred as the services are being provided by monitoring the status of the trial or project and the invoices received from our external service providers. We adjust our accrual as actual costs become known.

Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect that the levels of our research and development expenses will increase during the foreseeable future as we: (i) continue to advance Resolaris in clinical development; (ii) advance our Stalaris discovery program; and (iii) engage in additional research, discovery and development activities relating to our discovery engine for therapeutic applications of Physiocrines, including Project ORCA.

We cannot determine with certainty the timing of initiation, the duration or the completion costs of current or future preclinical studies and clinical trials of our product candidates. At this time, due to the inherently unpredictable nature of preclinical and clinical development and given the early stage of our programs, we are unable to estimate with any certainty the costs we will incur or the timelines we will require in the continued development of Resolaris, Stalaris and any other product candidates that we may develop. Clinical and preclinical development timelines, the probability of success and development costs can differ materially from expectations. We anticipate that we will make determinations as to which product candidates to pursue and how much funding to direct to each product candidate on an ongoing basis in response to the results of ongoing and future preclinical studies and clinical trials, regulatory developments and our ongoing assessments as to each product candidate's commercial potential. In addition, we cannot forecast which product candidates may be subject to future collaborations, when such arrangements will be secured, if at all, and to what degree such arrangements would affect our development plans and capital requirements.

General and Administrative Expenses

General and administrative expenses consist primarily of salaries and related costs for employees in executive, finance and administration, corporate development and administrative support functions, including stock-based compensation expenses and benefits. Other significant general and administrative expenses include accounting, legal services, expenses associated with applying for and maintaining patents, cost of insurance, cost of various consultants, occupancy costs, information systems costs and depreciation.

Other Income (Expense)

Other income (expense) consists primarily of interest income earned on cash and cash equivalents and available-for-sale investments and interest expense on our loans outstanding with Silicon Valley Bank (SVB). Commencing November 2016, interest expense includes interest charges from our Term Loan borrowing with SVB and Solar Capital Ltd. (Solar).

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States, or GAAP. 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 as of the date of the consolidated financial statements, as well as the reported expenses during the reporting periods. We monitor and analyze these items for changes in facts and circumstances, and material changes in these estimates could occur in the future. We base our estimates on our historical experience and on various other factors we believe to be 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. Changes in estimates are reflected in reported results for the period in which they become known. Actual results may differ materially from these estimates under different assumptions or conditions.

We discuss our accounting policies and assumptions that involve a higher degree of judgment and complexity within Note 2 to our audited consolidated financial statements appearing elsewhere in this Annual Report. We believe the following accounting policies related to research and development expense accruals and stock-based compensation involve the most significant estimation and judgment in accounting for our reported consolidated financial results.

Research and Development Expense Accruals

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued expenses. This process involves reviewing open contracts and purchase orders, communicating with our personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. The majority of our service providers invoice us monthly in arrears for services performed or when contractual milestones are met. We make estimates of our accrued expenses as of each balance sheet date in our consolidated financial statements based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. Examples of estimated accrued research and development expenses include fees paid to investigative sites and Clinical Research Organizations (CROs) in connection with clinical trials; service providers in connection with preclinical development activities; and service providers related to product manufacturing, development and distribution of clinical supplies.

We currently rely on third parties for the clinical development of Resolaris and Stalaris and the manufacture of Resolaris and Stalaris to support our ongoing and future clinical trials. We pay these third parties, including consultants, CROs, manufacturers and other service providers, pursuant to contractual arrangements, which may include provisions for time and materials-based payments, project-based fees and milestone payments. We base our accrual for these expenses on our estimates of the services received and efforts expended pursuant to our contractual arrangements. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our service providers will exceed the level of services provided and result in a prepayment of the clinical expense. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical milestones. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepaid accordingly.

Although we do not expect our estimates to be materially different from amounts actually incurred, if our estimates of the status and timing of services performed differs from the actual status and timing of services performed, we may report amounts that are too high or too low in any particular period. To date, there has been no material differences between our estimates and the amounts actually incurred.

Stock-Based Compensation

Stock-based compensation expense represents the grant date fair value of employee stock option grants recognized as expense over the requisite service period of the awards (usually the vesting period) on a straight-line basis, net of estimated forfeitures. For stock option grants with performance-based milestones, the expense is recorded over the service period after the achievement of the milestone is probable or the performance is achieved. For stock option grants with market-based conditions, the expense is recorded using the accelerated attribution method over the requisite service period for each vesting tranche. We account for stock options granted to non-employees using the fair value approach. These options are subject to periodic revaluation over their vesting terms. We estimate fair value of employee and non-employee stock option grants using the Black-Scholes option pricing model. We estimate the fair value of the market-based stock option grants using Monte Carlo simulations. We generally estimate the fair value using assumptions, including the risk-free interest rate, the expected volatility of a peer group of similar companies, the expected term of the awards and the expected dividend yield. These estimates involve inherent uncertainties and the application of management's judgment. If factors change and different assumptions are used, our stock-based compensation expense could be materially different in the future.

Results of Operations

Comparison of the Years Ended December 31, 2016 and 2015

The following table summarizes our results of operations for the years ended December 31, 2016 and 2015 (in thousands):

	Years Ended December 31,		Increase /
	2016	2015	(Decrease)
Research and development expenses	$ 42,846	$ 34,504	$ 8,342
General and administrative expenses	15,094	13,112	1,982
Other income (expense)	36	(357)	393

Research and development expenses. Research and development expenses were $42.8 million and $34.5 million for the years ended December 31, 2016 and 2015, respectively. The increase of $8.3 million was due primarily to a $3.2 million increase in clinical and non-clinical development costs for Resolaris, a $2.4 million increase in manufacturing development costs for Stalaris, a $2.0 million increase in other pre-clinical development costs, a $1.2 million increase related cGMP manufacturing of Resolaris to support future clinical trials and a $1.5 million increase related to compensation expenses resulting from increased headcount in research and development functions. The increase was offset by a decrease related to a one-time $1.4 million non-cash expense for the assignment of certain intellectual property rights in the prior year period and a $0.6 million reduction of non-cash stock-based compensation.

General and administrative expenses. General and administrative expenses were $15.1 million and $13.1 million for the years ended December 31, 2016 and 2015, respectively. The increase of $2.0 million was due primarily to a $1.8 million increase in personnel costs resulting from increased headcount, including $0.8 million of non-cash stock-based compensation.

Other income (expense). Other income (expense) was $36,000 and $(0.4) million for the years ended December 31, 2016 and 2015, respectively. The change was primarily a result of decreased interest expense from lower commercial debt balance during the current period as compared to the same period in the prior year.

Comparison of the Years Ended December 31, 2015 and 2014

The following table summarizes our results of operations for the years ended December 31, 2015 and 2014 (in thousands):

	Years Ended December 31,		Increase /
	2015	2014	(Decrease)
	(in thousands)		
Research and development expenses	$ 34,504	$ 16,777	$ 17,727
General and administrative expenses	13,112	6,777	6,335
Other income (expense)	(357)	(796)	439

Research and development expenses. Research and development expenses were $34.5 million and $16.8 million for the years ended December 31, 2015 and 2014, respectively. The increase of $17.7 million was due primarily to a $11.4 million increase related to manufacturing costs and clinical development incurred in support of various activities for Resolaris, a $4.1 million increase related to compensation expenses (including $2.0 million of non-cash stock-based compensation) as a result of increased headcount across our research and development organization and a $1.4 million increase related to the issuance of common stock in connection with the amendment and restatement of our research funding and option agreement with the The Scripps Research Institute, or TSRI.

General and administrative expenses. General and administrative expenses were $13.1 million and $6.8 million for the years ended December 31, 2015 and 2014, respectively. The increase of $6.3 million was due primarily to a $3.8 million increase in personnel costs resulting from increased headcount (including $1.1 million of non-cash stock-based compensation), a $1.7 million increase in costs associated with being a public company and a $0.3 million increase related to intellectual property-related projects.

Other income (expense). Other income (expense) was $(0.4) million and $(0.8) million for the years ended December 31, 2015 and 2014, respectively. The decrease of $0.4 million in other expense was primarily a result of $0.3 million increase in interest income related to short-term and long-term investments and a $0.1 million decrease in interest expense related to the $5.0 million we borrowed in June 2014 under a loan agreement with Silicon Valley Bank, or SVB.

Liquidity and Capital Resources

We have incurred losses and negative cash flows from operations since our inception. As of December 31, 2016, we had an accumulated deficit of $216.0 million and we expect to continue to incur net losses for the foreseeable future. As of December 31, 2016, we had cash, cash equivalents and available-for-sale investments of $76.1 million. We believe that our existing cash and cash equivalents as of December 31, 2016 will be sufficient to meet our anticipated cash requirements for a period of one year from the filing date of this Annual Report.

Sources of Liquidity

From our inception through December 31, 2016, we have funded our operations primarily with aggregate proceeds from the sales of our common stock through our IPO, the private placement of redeemable convertible preferred stock and convertible promissory notes and commercial bank debts.

Debt Financing

In each of July 2013 and June 2014, we borrowed $5.0 million under a $10.0 million loan and security agreement with SVB, which we refer to as the SVB Loan. Beginning in July 2014, we began to make payments of principal and interest which were due through the maturity date of June 1, 2017. The interest rate was a per annum fixed rate of 5.0% and 5.88% for the $5.0 million drawn in each of July 2013 and June 2014, respectively. This loan was repaid in full in November 2016 upon entering into the Term Loan discussed below.

On November 18, 2016, we entered into a loan and security agreement with SVB and Solar, which we refer to as the Term Loan. SVB and Solar agreed to lend us up to $20.0 million, issuable in three separate tranches of: (i) $10.0 million which was funded on November 18, 2016; (ii) $5.0 million may be drawn down by us at any time before the earlier of June 30, 2017 or an event of default, at our discretion, subject to achievement of certain financial and clinical milestones; and (iii) $5.0 million may be drawn down by us any time after June 30, 2017 and before the earlier of December 31, 2017 or an event of default, at our discretion, subject to achievement of certain milestones specified for the second tranche and additional financial and clinical milestones.

We will make interest only payments through December 1, 2017 or June 1, 2018, if we draw the second tranche, followed by consecutive equal monthly payments of principal and interest in arrears through the maturity date of November 18, 2020. The Term Loan provides for an interest rate equal to the sum of the prime rate, as reported in The Wall Street Journal on the last date of the month preceding the month in which interest will accrue, plus 4.10%. The Term Loan also provides for a final interest payment equal to 8.75% of the funded amount, which is due when the Term Loan becomes due or upon the prepayment of the loan. We have the option to prepay the outstanding balance of the loan in full, subject to a prepayment fee ranging from 1.0% to 3.0% depending upon when the prepayment occurs, including any non-usage fees. The Term Loan provides for a 2.0% non-usage fee for any unfunded amount in the event we do not draw the second tranche and third tranche, payable no later than the expiration date for the second tranche or third tranche, as applicable, or the date of cancellation of the loan due to prepayment or an event of default.

In connection with the Term Loan, we issued warrants to each of SVB and Solar to purchase an aggregate of 47,771 shares of our common stock with an exercise price of $3.14 per share. The warrants are immediately exercisable and will expire on November 18, 2023, provided that such warrants have not been previously exercised or have expired in connection with certain fundamental transactions involving us.

Of the $10.0 million funded in the first tranche of the Term Loan, approximately $2.6 million was used to repay in full our principal and interest obligations under the SVB Loan. We did not pay any termination or other fees in connection with the repayment of amounts due under the SVB Loan.

Cash Flows

The following table sets forth a summary of the net cash flow activity for each of the periods indicated (in thousands):

	Years Ended December 31,		
	2016	2015	2014
Net cash provided by (used in):			
Operating activities	$ (52,861)	$ (36,797)	$ (22,824)
Investing activities	33,527	(71,994)	(2,246)
Financing activities	4,697	147,917	2,512
Net increase (decrease) in cash	$ (14,637)	$ 39,126	$ (22,558)

Operating activities. Net cash used in operating activities was $52.9 million, $36.8 million and $22.8 million for the years ended December 31, 2016, 2015 and 2014, respectively. The net cash used in operating activities in each of these periods was primarily due to our net losses. The primary differences between net cash used in operating activities and our net loss in the year ended December 31, 2016 related to non-cash charges including $0.9 million for depreciation and $5.0 million for stock-based compensation and $1.4 million of cash used by changes in our prepaid and other assets, accounts payable and accrued expense accounts. The primary differences between net cash used in operating activities and our net loss in the year ended December 31, 2015 related to non-cash charges including: $0.9 million for depreciation, $4.9 million for stock-based compensation, $1.4 million for the issuance of common stock for technology to TSRI and $3.3 million of cash provided by changes in our prepaid and other assets, accounts payable and accrued expense accounts. The primary differences between net cash used in operating activities and our net loss in the year ended December 31, 2014 related to non-cash charges including: $0.8 million for depreciation and amortization, $1.8 million for stock-based compensation offset by $1.3 million of cash used by changes in our prepaid and other assets, accounts payable and accrued expense accounts.

Investing activities. Net cash provided by investing activities for the year ended December 31, 2016 consisted of $34.1 million of net maturities of investment securities and $0.6 million of property and equipment purchases. Net cash used in investing activities for the year ended December 31, 2015 consisted of $71.3 million of net purchases of investment securities and $0.7 million of property and equipment purchases. Net cash used in investing activities for the year ended December 31, 2014 consisted of $2.0 million of net purchases of investments and $0.2 million of property and equipment purchases.

Financing activities. Net cash provided by financing activities for the year ended December 31, 2016 was $4.7 million and consisted primarily of $9.7 million of net proceeds from the Term Loan offset by $5.2 million of principal payments. Net cash provided by financing activities for the year ended December 31, 2015 was $147.9 million and consisted primarily of $75.6 million of net proceeds from the issuance of Series E redeemable convertible preferred stock and $76.9 million of proceeds from the IPO net of offering costs paid in the period, offset by $3.2 million of principal payments on the SVB Loan and $2.0 million repayment of convertible debt and related accrued interest. Net cash provided by financing activities during the year ended December 31, 2014 was $2.5 million and consisted primarily of $5.0 million of proceeds from the SVB Loan offset by $1.6 million of principal payments on the SVB Loan and $1.0 million of costs paid in connection with our planned initial public offering.

Funding Requirements

To date, we have not generated any revenues from product sales. We expect our expenses to increase in connection with our ongoing activities, particularly as we continue to advance Resolaris in clinical development, continue our research and development activities with respect to potential Physiocrine-based therapeutics, and seek marketing approval for Resolaris and other product candidates that we may develop. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. We currently have no sales or marketing capabilities and would need to expand our organization to support these activities. Furthermore, we expect to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. Our forecast of the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement that involves risks and uncertainties, and actual results could vary materially.

Our future capital requirements are difficult to forecast and will depend on many factors, including:

- our ability to initiate, and the progress and results of, our planned clinical trials of Resolaris;
- the scope, progress, results and costs of preclinical development, and clinical trials for our other product candidates;
- the costs, timing and outcome of regulatory review of our product candidates;
- the costs and timing of preparing, filing and prosecuting patent applications, maintaining and enforcing our intellectual property rights and defending any intellectual property-related claims;
- the costs and timing of future commercialization activities, including product manufacturing, marketing, sales and distribution, for any of our product candidates for which we receive marketing approval; and
- the extent to which we acquire or in-license other products and technologies.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic partnerships and/or licensing arrangements. To the extent we raise additional capital through the sale of equity or convertible debt securities, the ownership interest of our stockholders will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect the rights of our common stockholders. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through collaborations, strategic partnerships or licensing arrangements with third parties, we may have to relinquish valuable rights to our product candidates, our other technologies, future revenue streams or research programs or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market our product candidates even if we would otherwise prefer to develop and market such product candidates ourselves.

Contractual Obligations and Commitments

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

		Payments Due by Period			
	Total	Less than 1 Year	1-3 Years	3-5 Years	More than 5 Years
		(in thousands)			
Term Loan, principal payments including final payment	$ 10,875	$ 249	$ 6,448	$ 4,178	$ —
Operating lease (1)	386	386	—	—	—
Total	$ 11,261	$ 635	$ 6,448	$ 4,178	$ —

(1) Our operating lease obligations relate to our corporate headquarters in San Diego, California. We lease 17,083 square feet of office and laboratory space under an operating lease that expires in May 2017 and 7,411 square feet we subleased from a tenant of our landlord that expires in June 2017. In January 2017, we extended our primary facility lease with our landlord through May 2019 for an additional commitment of $1.5 million.

We enter into contracts in the normal course of business with clinical trial sites and clinical supply manufacturing organizations and with vendors for preclinical safety and research studies, research supplies and other services and products purposes. These contracts generally provide for termination after a notice period, and therefore are cancelable contracts and not included in the table of contractual obligations and commitments.

We may have payment obligations under our agreements with TSRI certain of which are contingent upon future events such as our achievement of specified development, regulatory and commercial milestones, and we are required to make development milestone payments and royalty payments in connection with the sale of products developed under these agreements. As of December 31, 2016, we were unable to estimate the timing or likelihood of achieving the milestones or making future product sales and, therefore, any related payments are not included in the table above.

We are party to an amended and restated research funding and option agreement with TSRI, under which we provide funding to TSRI to conduct certain research activities related to aminoacyl tRNA synthetases. Under the research funding and option agreement, TSRI has granted us options to enter into license agreements to acquire rights and exclusive licenses to develop, make, have made, use, have used, import, have imported, offer to sell, sell and have sold certain licensed products, processes and services based on certain technology arising from the sponsored research activities. Pursuant to the terms of these license agreements, TSRI is entitled to receive tiered royalties as a percentage of net sales, ranging from the low to mid-single digits, with these royalty rates subject to adjustment under certain circumstances. Additionally, we have agreed to pay TSRI a percentage of non-royalty revenue we receive from our sublicensees or partners, with the amount owed decreasing if we enter into the applicable sublicense agreement or partnering agreement after meeting a specified clinical milestone. We are obligated to make payments to TSRI of up to an aggregate of $2.75 million under each license agreement upon the achievement of specific clinical and regulatory milestone events.

We have payment obligations under our agreement with FUJIFILM Diosynth Biotechnologies, U.S.A., Inc. (Fujifilm) related to development and production milestones of up to the mid seven figures for process optimization, scale-up and demonstration, and cGMP manufacturing of the drug substance of Resolaris. In addition, we are billed for consumables on a pass-through basis. In the next 12 months, we are committed to pay Fujifilm approximately $0.6 million based on development and production milestones.

In addition, we have payment obligations under our agreement with a third party contracted development and manufacturing organization of up to low seven figures related to the development of the manufacturing process and for the production of drug substance for Stalaris. In the next 12 months, we are committed to pay the third party contract manufacturing organization approximately $2.2 million based on development and production milestones.

Recent Accounting Pronouncements

For discussion of recently issued accounting pronouncements, refer to the Section titled "Recently Accounting Pronouncements" within Note 2 of our financial statements included in this Annual Report.

Off-Balance Sheet Arrangements

We did not have during the periods presented, and we do not currently have, any off-balance sheet arrangements, as defined in the rules and regulations of the SEC.

JOBS Act

In April 2012, the JOBS Act was enacted. Section 107 of the JOBS Act provides that an emerging growth company can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act for complying with new or revised accounting standards. Thus, an emerging growth company can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this extended transition period and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other companies.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

Interest Rate Risk

We are exposed to market risk related to changes in interest rates. As of December 31, 2016, we had cash and cash equivalents, and available-for-sale investments totaling of $76.1 million. We invest our excess cash in investment-grade, interest-bearing securities. The primary objective of our investment activities is to preserve principal and liquidity. To achieve this objective, we invest in money market funds, U.S. treasury and high quality marketable debt instruments of corporations and financial institutions, government sponsored and asset backed securities with contractual maturity dates of less than two years. If interest rates were to increase instantaneously and uniformly by 100 basis points, compared to interest rates as of December 31, 2016, the increase would not have had a material effect on the fair market value of our portfolio.

We do not believe that our cash, cash equivalents and investments have significant risk of default or illiquidity. While we believe our cash and cash equivalents do not contain excessive risk, we cannot provide absolute assurance that in the future our investments will not be subject to adverse changes in market value. In addition, we maintain significant amounts of cash and cash equivalents at one or more financial institutions that are in excess of federally insured limits.

Our Term Loan bears interest at variable rates equal to the sum of the prime rate, as reported in the Wall Street Journal on the last date of the month preceding the month in which interest will accrue, plus 4.10%. Accordingly, increases in these published rates would increase our interest payments under the Term Loan. A one percentage point increase in interest rates would increase expense by approximately $0.1 million annually and would not materially affect our results of operations.

Foreign Currency Exchange Risk

We incur expenses, including for CROs and clinical trial sites, outside the United States based on contractual obligations denominated in currencies other than the U.S. dollar, including Pounds Sterling and Euro. At the end of each reporting period, these liabilities are converted to U.S. dollars at the then-applicable foreign exchange rate. As a result, our business is affected by fluctuations in exchange rates between the U.S. dollar and foreign currencies. We do not enter into foreign currency hedging transactions to mitigate our exposure to foreign currency exchange risks. Exchange rate fluctuations may adversely affect our expenses, results of operations, financial position and cash flows. Recently, the Pounds Sterling has experienced higher volatility as a result of the British political decision to leave the European Union (Brexit). However, to date, fluctuations including those related to Brexit have not had a significant impact to us and a movement of 10% in the U.S. dollar to Pounds Sterling or U.S. dollar to Euro exchange rates would not have a material effect on our results of operations or financial condition.

Effects of Inflation

Inflation generally affects us by increasing our cost of labor, manufacturing, clinical trial, and other research and development and administration costs. We do not believe that inflation has had a material effect on our results of operations or financial condition during the periods presented.

Item 8. Financial Statements and Supplementary Data

Report of Independent Registered Public Accounting Firm

The Board of Directors and Stockholders of
aTyr Pharma, Inc.

We have audited the accompanying consolidated balance sheets of aTyr Pharma, Inc. as of December 31, 2016 and 2015, and the related consolidated statements of operations, comprehensive loss, stockholders' equity (deficit) and cash flows for each of the three years in the period ended December 31, 2016. 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 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. We were not engaged to perform an audit of the Company's internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion. An audit also 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.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of aTyr Pharma, Inc. at December 31, 2016 and 2015, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2016, in conformity with U.S. generally accepted accounting principles.

/s/ Ernst & Young LLP
San Diego, California
March 16, 2017

aTyr Pharma, Inc.
Consolidated Balance Sheets
(in thousands, except share and per share data)

	December 31,	
	2016	**2015**
Assets		
Current assets:		
Cash and cash equivalents	$ 38,388	$ 53,025
Available-for sale investments, short-term	33,759	42,510
Prepaid expenses and other assets	2,621	2,415
Total current assets	74,768	97,950
Available-for sale investments, long-term	4,002	29,814
Property and equipment, net	1,421	1,793
Other assets	333	118
Total assets	$ 80,524	$ 129,675
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 2,606	$ 3,872
Accrued expenses	5,450	4,595
Current portion of deferred rent	130	315
Current portion of long-term debt	339	3,366
Total current liabilities	8,525	12,148
Deferred rent, net of current portion	—	130
Long-term debt, net of current portion and issuance costs	9,198	1,776
Other long-term liabilities	—	571
Commitments and contingencies (Note 5)		
Stockholders' equity:		
Common stock, $0.001 par value; authorized shares – 150,000,000 and 95,500,000 at December 31, 2016 and 2015, respectively; issued and outstanding shares – 23,744,832 and 23,670,079 at December 31, 2016 and 2015, respectively	24	24
Additional paid-in capital	278,832	273,321
Accumulated other comprehensive loss	(76)	(171)
Accumulated deficit	(215,979)	(158,124)
Total stockholders' equity	62,801	115,050
Total liabilities and stockholders' equity	$ 80,524	$ 129,675

See accompanying notes.

aTyr Pharma, 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	$ 42,846	$ 34,504	$ 16,777
General and administrative	15,094	13,112	6,777
Total operating expenses	57,940	47,616	23,554
Loss from operations	(57,940)	(47,616)	(23,554)
Interest income (expense), net	65	(386)	(832)
Loss on extinguishment of debt	(29)	—	—
Change in fair value of warrant liabilities	—	29	36
Total other income (expense)	36	(357)	(796)
Loss before income taxes	(57,904)	(47,973)	(24,350)
Income tax benefit	49	—	—
Net loss	(57,855)	(47,973)	(24,350)
Accretion to redemption value of redeemable convertible preferred stock	—	(15)	(416)
Net loss attributable to common stockholders	(57,855)	(47,988)	(24,766)
Net loss per share attributable to common stockholders, basic and diluted	$ (2.44)	$ (3.03)	$ (29.69)
Weighted average common stock shares outstanding, basic and diluted	23,681,019	15,838,353	834,221

See accompanying notes.

aTyr Pharma, Inc.
Consolidated Statements of Comprehensive Loss
(in thousands)

	Year Ended December 31,		
	2016	**2015**	**2014**
Net loss	$ (57,855)	$ (47,973)	$ (24,350)
Other comprehensive gain (loss):			
Change in unrealized gain (loss) on available for sale investments, net of tax	95	(171)	—
Comprehensive loss	$ (57,760)	$ (48,144)	$ (24,350)

See accompanying notes.

aTyr Pharma, Inc.
Consolidated Statements of Stockholders' Equity (Deficit)
(in thousands, except share data)

	Redeemable Convertible Preferred Stock		Common Stock		Additional Paid-In Capital	Stockholder Note Receivable	Non-Controlling Interest	Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount						
Balance as of December 31, 2013	73,487,415	$ 93,165	856,591	$ 1	$ 17,373	$ (69)	$ 2,414	$ —	$ (85,801)	$ (66,082)
Exercise of common stock options	—	—	53,289	—	43	—	29	—	—	72
Changes in share repurchase liability	—	—	—	—	13	—	—	—	—	13
Stock-based compensation	—	—	—	—	1,791	—	—	—	—	1,791
Dissolution of affiliates	—	2,038	—	—	405	—	(2,443)	—	—	(2,038)
Accretion to redemption value of redeemable convertible preferred stock	—	416	—	—	(416)	—	—	—	—	(416)
Net loss	—	—	—	—	—	—	—	—	(24,350)	(24,350)
Balance as of December 31, 2014	73,487,415	95,619	909,880	1	19,209	(69)	—	—	(110,151)	(91,010)
Issuance of Series E redeemable convertible preferred stock for cash	68,166,894	75,650	—	—	—	—	—	—	—	—
Conversion of redeemable convertible preferred stock in connection with initial public offering	(141,654,309)	(171,284)	16,279,859	16	171,268	—	—	—	—	171,284
Issuance of common stock through initial public offering, net	—	—	6,164,000	6	75,897	—	—	—	—	75,903
Repayment of stockholder note receivable	—	—	—	—	(9)	69	—	—	—	60
Exercise of common stock options	—	—	196,500	1	534	—	—	—	—	535
Reclassification of preferred stock warrant liability to additional paid-in-capital	—	—	—	—	290	—	—	—	—	290
Issuance of common stock to The Scripps Research Institute	—	—	119,840	—	1,411	—	—	—	—	1,411
Changes in share repurchase liability	—	—	—	—	(120)	—	—	—	—	(120)
Stock-based compensation	—	—	—	—	4,856	—	—	—	—	4,856
Accretion to redemption value of redeemable convertible preferred stock	—	15	—	—	(15)	—	—	—	—	(15)
Net unrealized loss on investments	—	—	—	—	—	—	—	(171)	—	(171)
Net loss	—	—	—	—	—	—	—		(47,973)	(47,973)
Balance as of December 31, 2015	—	—	23,670,079	24	273,321	—	—	(171)	(158,124)	115,050
Exercise of common stock options	—	—	17,972	—	20	—	—	—	—	20
Issuance of common stock pursuant to employee stock purchase plan	—	—	56,781	—	143	—	—	—	—	143
Issuance of warrants related to term loan	—	—	—	—	217	—	—	—	—	217
Changes in share repurchase liability	—	—	—	—	102	—	—	—	—	102
Stock-based compensation	—	—	—	—	5,029	—	—	—	—	5,029
Net unrealized gain on investments, net of tax	—	—	—	—	—	—	—	95	—	95
Net loss	—	—	—	—	—	—	—	—	(57,855)	(57,855)
Balance as of December 31, 2016	—	—	23,744,832	$ 24	$ 278,832	$ —	$ —	$ (76)	$ (215,979)	$ 62,801

See accompanying notes.

aTyr Pharma, Inc.
Consolidated Statements of Cash Flows
(in thousands)

	Year Ended December 31,		
	2016	**2015**	**2014**
Cash flows from operating activities:			
Net loss	$ (57,855)	$ (47,973)	$ (24,350)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	900	869	829
Issuance of common stock for technology	—	1,411	—
Stock-based compensation	5,029	4,856	1,791
Amortization of debt discount	173	297	426
Loss on debt extinguishment	29	—	—
Change in fair value of preferred stock warrant liability	—	(29)	(36)
Amortization of premium of available-for-sale investment securities	531	789	43
Deferred rent	(315)	(295)	(277)
Changes in operating assets and liabilities			
Prepaid expenses and other assets	(421)	(666)	(1,043)
Accounts payable and accrued expenses	(932)	3,944	(207)
Net cash used in operating activities	(52,861)	(36,797)	(22,824)
Cash flows from investing activities:			
Purchase of property and equipment	(600)	(664)	(249)
Purchases of available-for-sale investment securities	(28,089)	(109,445)	(5,397)
Maturities of available-for-sale investment securities	62,216	38,115	3,400
Net cash provided by (used in) investing activities	33,527	(71,994)	(2,246)
Cash flows from financing activities:			
Issuance of preferred stock for cash, net of issuance costs	—	75,648	—
Issuance of common stock through initial public offering, net of offering costs	—	76,902	—
Costs paid in connection with initial public offering	—	—	(999)
Proceeds from issuance of common stock through option exercises	20	604	72
Proceeds from employee stock purchase plan	143	—	—
Proceeds from borrowing, net	9,736	—	5,000
Repayments on notes payable to bank	(5,202)	(3,237)	(1,561)
Repayment of convertible debt	—	(2,000)	—
Net cash provided by financing activities	4,697	147,917	2,512
Net change in cash and cash equivalents	(14,637)	39,126	(22,558)
Cash and cash equivalents at beginning of year	53,025	13,899	36,457
Cash and cash equivalents at the end of year	$ 38,388	$ 53,025	$ 13,899
Supplemental disclosure of cash flow information:			
Interest paid	$ 225	$ 925	$ 415
Supplemental schedule of noncash investing and financing activities:			
Issuance of warrants in connection with borrowings	$ 217	$ —	$ 148
Changes in share repurchase liability	$ 102	$ (120)	$ 13

See accompanying notes.

1. Organization, Business and Basis of Presentation

Organization and Business

We were incorporated in the state of Delaware on September 8, 2005. We are focused on the discovery and clinical development of innovative medicines for patients suffering from severe, rare diseases.

Principles of Consolidation

Our consolidated financial statements include our accounts, our 98% majority-owned subsidiary in Hong Kong, Pangu BioPharma Limited (Pangu BioPharma). All intercompany transactions and balances are eliminated in consolidation.

Use of Estimates

Our consolidated financial statements are prepared in accordance with generally accepted accounting principles (GAAP). The preparation of our consolidated financial statements requires us to make estimates and assumptions that impact the reported amounts of assets, liabilities and expenses and the disclosure of contingent assets and liabilities in our consolidated financial statements and accompanying notes. The most significant estimates in our consolidated financial statements relate to the fair value of equity issuances and awards, and clinical trial and research and development expenses. Although these estimates are based on our knowledge of current events and actions we may undertake in the future, actual results may ultimately differ materially from these estimates and assumptions.

Segment Reporting

Operating segments are identified as components of an enterprise about which separate discrete financial information is available for evaluation by the chief operating decision-maker in making decisions regarding resource allocation and assessing performance. We view our operations and manage our business in one operating segment.

2. Summary of Significant Accounting Policies

Cash and Cash Equivalents

Cash and cash equivalents consist primarily of readily available checking, money market accounts and money market funds. We consider all highly liquid investments that mature in three months or less when purchased to be cash equivalents.

Investment Securities

Investment securities primarily consist of investment grade corporate debt securities, asset-backed securities, commercial paper and United States Treasury securities. We classify all investment securities as available-for-sale. Investment securities are carried at fair value, with the unrealized gains and losses, if any, reported as a component of other comprehensive income (loss) in stockholders' equity (deficit) until realized. Realized gains and losses from the sale of investment securities, if any, are determined on a specific identification basis. A decline in the market value of any investment security below cost that is determined to be other than temporary will result in an impairment charge to earnings and a new cost basis for the security is established. No such impairment charges were recorded for any period presented. Premiums and discounts are amortized or accreted over the life of the related security as an adjustment to yield using the straight-line method and are included in interest income. Interest income is recognized when earned. As of December 31, 2016, we held an aggregate total of $37.8 million of investment securities which consisted of corporate debt securities, asset-backed securities, commercial paper and United States Treasury securities, all of which will mature in less than one year and there was a $27,000 difference between the amortized cost and fair value of these investment securities. As of December 31, 2015, we held $72.3 million of corporate debt securities, all of which mature in less than two years, and there was $0.2 million difference between the amortized cost and fair value of these investment securities.

Concentration of Credit Risk

Financial instruments that potentially subject us to significant concentration of credit risk consist primarily of cash, cash equivalents and investment securities. We have established guidelines regarding diversification of investments and their maturities, which are designed to maintain principal and maximize liquidity. We maintain deposits in federally insured financial institutions in excess of federally insured limits. We have not experienced any losses in such accounts and we believe that we are not exposed to significant credit risk due to the financial position of the depository institutions in which those deposits are held.

Property and Equipment

Property and equipment are stated at cost and depreciated on a straight-line basis over the estimated useful life of the related assets (generally three to seven years). Leasehold improvements are stated at cost and amortized on a straight-line basis over the lesser of the remaining term of the related lease or the estimated useful life of the leasehold improvements. Repairs and maintenance costs are charged to expense as incurred.

Impairment of Long-Lived Assets

Long-lived assets consist primarily of property and equipment. An impairment loss is recorded if and when events and circumstances indicate that assets might be impaired and the undiscounted cash flows estimated to be generated by those assets are less than the carrying amount of those assets. While our current and historical operating losses are indicators of impairment, we believe that future cash flows to be received support the carrying value of our long-lived assets and, accordingly, have not recognized any impairment losses since inception.

Accrued Expenses

As part of the process of preparing our consolidated financial statements, we are required to estimate accrued expenses, including accrued research and development expenses for fees paid to investigative sites and CROs in connection with clinical trials; service providers in connection with preclinical development activities; service providers related to product manufacturing; and other professional services. The accrual process involves reviewing open contracts and purchase orders, communicating with our personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. We make estimates of accrued expenses as of each balance sheet date in our consolidated financial statements based on facts and circumstances known to us at that time. Although we do not expect the estimates to be materially different from amounts actually incurred, if the estimates of the status and timing of services performed differs from the actual status and timing of services performed, we may report amounts that are too high or too low in any particular period.

Deferred Rent

Rent expense, including the value of tenant improvement allowances received, is recorded on a straight-line basis over the term of the lease. The difference between rent expense and amounts paid under the lease agreements is recorded as deferred rent in the accompanying consolidated balance sheets.

Research and Development Costs

Research and development costs are expensed as incurred. Research and development costs include: salaries and employee-related expenses, including stock-based compensation and benefits for personnel in research and product development functions; costs associated with conducting our preclinical, development and regulatory activities, including fees paid to third-party professional consultants, service providers and our scientific, therapeutic and clinical advisory boards; costs to acquire, develop and manufacture preclinical study and clinical trial materials; costs incurred under clinical trial agreements with clinical research organizations and investigative sites; costs for laboratory supplies; payments related to licensed products and technologies; allocated facilities and information technology costs; and depreciation.

Patent Costs

Costs related to filing and pursuing patent applications are recorded as general and administrative expense and expensed as incurred since recoverability of such expenditures is uncertain.

Stock-Based Compensation

Stock-based compensation expense represents the cost of the grant date fair value of employee stock option and restricted stock unit grants recognized over the requisite service period of the awards (usually the vesting period) on a straight-line basis and the cost of the fair value of restricted stock units recognized over the requisite period. We recognize forfeitures as they occur as a reduction of expense. For stock option grants with performance-based milestones, the expense is recorded over the service period after the achievement of the milestone is probable or the performance condition is achieved. For stock option grants with market-based conditions, the expense is recorded using the accelerated attribution method over the requisite service period for each vesting tranche. We account for stock options granted to non-employees using the fair value approach. These option grants are subject to periodic revaluation over their vesting terms. We estimate the fair value of employee and non-employee stock option grants using the Black-Scholes option pricing model. We estimate the fair value of the market-based stock option grants using a Monte Carlo simulation. The fair value of restricted stock units is determined by the closing price as of the grant date.

Income Taxes

We account for income taxes under the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the financial statements. Under this method, deferred tax assets and liabilities are determined on the basis of the differences between the financial statements and tax basis of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. The effect of a change in tax rates on deferred tax assets and liabilities is recognized as income in the period that includes the enactment date.

We recognize net deferred tax assets to the extent that we believe these assets are more likely than not to be realized. In making such a determination, we consider all available positive and negative evidence, including future reversals of existing taxable temporary differences, projected future taxable income, tax-planning strategies and results of recent operations. If we determine that we would be able to realize the deferred tax assets in the future in excess of their net recorded amount, we would make an adjustment to the deferred tax asset valuation allowance, which would reduce the provision for income taxes.

We record uncertain tax positions on the basis of a two-step process whereby (1) we determine whether it is more likely than not that the tax positions will be sustained on the basis of the technical merits of the position and (2) for those tax positions that meet the more-likely-than-not recognition threshold, we recognize the largest amount of tax benefit that is more than 50% likely to be realized upon ultimate settlement with the related tax authority. We recognize interest and penalties related to unrecognized tax benefits within income tax expense. Any accrued interest and penalties are included within the related tax liability.

In November 2015, the Financial Accounting Standards Board (FASB) issued Accounting Standards Update (ASU) No. 2015-17, *Balance Sheet Classification of Deferred Taxes*, which requires all deferred tax assets and liabilities to be classified as noncurrent on the balance sheet. The new accounting guidance is effective for annual reporting periods beginning after December 15, 2016 and interim periods therein. Early adoption is permitted as of the beginning of interim or annual reporting periods. We elected to early adopt this guidance prospectively beginning in the year ended December 31, 2015 and prior periods were not retrospectively adjusted. There was no material impact on the financial statements upon adoption.

In March 2016, the FASB issued ASU No. 2016-09, *Compensation-Stock Compensation (Topic 718): Improvements to Employee Share-Based Payment Accounting*, which involves several aspects of the accounting for share-based payment transactions, including income tax consequences, classification of awards as either equity or liabilities, and classification on the statement of cash flows. ASU 2016-09 will be effective for the annual periods beginning after December 15, 2016 and interim periods within those annual periods, with early adoption permitted. We elected to early adopt this guidance beginning in the year ended December 31, 2016. Upon adoption, the balance of the unrecognized excess tax benefits will be reversed with the impact recorded to retained earnings net of any change to the valuation allowance as a result of the adoption. Due to the full valuation allowance on the U.S. deferred tax assets, there was no material impact in our consolidated financial position or results of operations upon adoption.

Net Loss Per Share

Basic net loss per share is calculated by dividing the net loss attributable to common stockholders by the weighted average number of common shares outstanding for the period, without consideration for common stock equivalents and adjusted for the weighted average number of common shares outstanding that are subject to repurchase. We have excluded 25,984, 61,814 and 61,457 shares subject to repurchase from the weighted average number of common shares outstanding for the years ended December 31, 2016, 2015 and 2014, respectively. Diluted 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 common stock equivalents outstanding for the period determined using the treasury-stock method. Dilutive common stock equivalents are comprised of redeemable convertible preferred stock, redeemable convertible preferred stock issuable upon conversion of convertible promissory note, warrants for the purchase of redeemable convertible preferred stock, warrants for common stock and options outstanding under our stock option plan. For all periods presented, there is no difference in the number of shares used to calculate basic and diluted shares outstanding due to our net loss position.

Potentially dilutive securities not included in the calculation of diluted net loss per share because to do so would be anti-dilutive are as follows (in common share equivalents):

	Year Ended December 31,		
	2016	2015	2014
Redeemable convertible preferred stock outstanding	—	—	9,238,868
Redeemable convertible preferred stock issuable upon conversion of convertible promissory note	—	—	94,455
Warrants for redeemable convertible preferred stock	—	—	25,970
Warrants for common stock	121,512	25,970	—
Common stock options and awards	4,091,701	2,625,280	1,514,471
Employee stock purchase plan	36,836	17,363	—
	4,250,049	2,668,613	10,873,764

The following table summarizes our net loss per share (in thousands, except per share data):

	Year Ended December 31,		
	2016	2015	2014
Numerator:			
Consolidated net loss	$ (57,855)	$ (47,973)	$ (24,350)
Accretion to redemption value	—	(15)	(416)
Net loss attributable to common stockholders	(57,855)	(47,988)	(24,766)
Denominator:			
Weighted average common shares outstanding	23,707,003	15,900,167	895,678
Weighted average common shares subject to repurchase	(25,984)	(61,814)	(61,457)
Weighted average common shares outstanding - basic and diluted	23,681,019	15,838,353	834,221
Net loss per share - basic and diluted	$ (2.44)	$ (3.03)	$ (29.69)

Recent Accounting Pronouncements

In August 2014, the Financial Accounting Standards Board (FASB) issued Accounting Standards Update (ASU) No. 2014-15, *Presentation of Financial Statements — Going Concern (Subtopic 205-40): Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern*. ASU 2014-15 provides that in connection with preparing financial statements for each annual and interim reporting period, an entity's management should evaluate whether there are conditions or events, considered in the aggregate, that raise substantial doubt about the entity's ability to continue as a going concern within one year after the date that the financial statements are issued (or within one year after the date that the financial statements are available to be issued when applicable). ASU 2014-15 is effective for the annual reporting period ending after December 15, 2016, and for annual and interim periods thereafter. Early adoption is permitted. The adoption of this guidance did not affect our consolidated financial position or results of operations.

In April 2015, the FASB issued ASU No. 2015-03, *Interest - Imputation of Interest (Subtopic 835-30): Simplifying the Presentation of Debt Issuance Costs*. ASU 2015-03 requires that debt issuance costs related to a recognized debt liability be presented in the balance sheet as a direct deduction from that debt liability, consistent with the presentation of a debt discount. The recognition and measurement guidance for debt issuance costs is not affected by ASU 2015-03. ASU 2015-03 is effective for fiscal years beginning after December 15, 2015, and interim periods within those fiscal years. We adopted ASU 2015-03 in January 2016 and the guidance did not affect our consolidated financial position or results of operations.

In January 2016, the FASB issued ASU No. 2016-01, *Financial Instruments-Overall: Recognition and Measurement of Financial Assets and Financial Liabilities*, which requires that (i) all equity investments, other than equity-method investments, in unconsolidated entities generally be measured at fair value through earnings and (ii) when the fair value option has been elected for financial liabilities, changes in fair value due to instrument-specific credit risk will be recognized separately in other comprehensive income. Additionally, ASU 2016-01 changes the disclosure requirements for financial instruments. The new standard will be effective for fiscal years beginning after December 15, 2018, and interim periods within fiscal years beginning after December 15, 2019. Early adoption is permitted for certain provisions. The adoption of ASU 2015-03 is not expected to have a material impact on our consolidated financial position or results of operations.

In February 2016, the FASB issued ASU No. 2016-02, *Leases (Topic 842)*, to increase transparency and comparability among organizations by requiring recognition of lease assets and lease liabilities on the balance sheet and disclosure of key information about leasing arrangements. The new standard will become effective for interim and annual periods beginning after December 15, 2018, with early adoption permitted, and is required to be adopted at the earliest period presented using a modified retrospective approach. We are currently evaluating the impact the provisions will have on our consolidated financial position or results of operations and whether we will adopt the guidance early.

In March 2016, the FASB issued ASU No. 2016-09, *Compensation-Stock Compensation(Topic 718): Improvements to Employee Share-Based Payment Accounting*, which involves several aspects of the accounting for share-based payment transactions, including income tax consequences, classification of awards as either equity or liabilities, and classification on the statement of cash flows. ASU 2016-09 will be effective for the annual periods beginning after December 15, 2016 and interim periods within those annual periods, with early adoption permitted. We elected to early adopt this guidance prospectively beginning in the year ended December 31, 2016. There was no material impact on the financial position or results of operations upon adoption.

In June 2016, the FASB issued ASU 2016-13, *Financial Instruments-Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments*, which provides financial statement users with more decision-useful information about the expected credit losses on financial instruments and other commitments to extend credit held by a reporting entity at each reporting date. To achieve this objective, the amendments in this Update replace the incurred loss impairment methodology in current GAAP with a methodology that reflects expected credit losses and requires consideration of a broader range of reasonable and supportable information to inform credit loss estimates. ASU 2016-13 will be effective for the annual periods beginning after December 15, 2019 and interim periods within those annual periods, with early adoption permitted beginning after December 15, 2018. We are currently evaluating the impact the provisions will have on our consolidated financial position or results of operations.

In August 2016, the FASB issued ASU 2016-15, *Statement of Cash Flows (Topic 230), Classification of Certain Cash Receipts and Cash Payments* which addresses eight specific cash flow issues to reduce the existing diversity in practice. The cash flow issues include debt prepayment or debt extinguishment costs, settlement of zero-coupon debt instruments or other debt instruments with coupon interest rates that are insignificant in relation to the effective interest rate of the borrowing, contingent consideration payments made after a business combination, proceeds from the settlement of insurance claims, proceeds from the settlement of corporate-owned life insurance policies, including bank-owned life insurance policies, distributions received from equity method investees, beneficial interests in securitization transactions and separately identifiable cash flows and application of the predominance principle. ASU 2016-15 will be effective for the annual periods beginning after December 15, 2017 and interim periods within those annual periods, with early adoption permitted. We adopted ASU 2016-15 for the year-ended December 31, 2016. The adoption of this guidance did not have a material impact on our consolidated financial position or results of operations.

3. Fair Value Measurements

The carrying amounts of cash equivalents, prepaid and other assets, accounts payable and accrued liabilities are considered to be representative of their respective fair values because of the short-term nature of those instruments. Based on the borrowing rates currently available to us for loans with similar terms, which is considered a Level 2 input, we believe that the fair value of our Term Loan approximates its carrying values. Investment securities are recorded at fair value.

The accounting guidance defines fair value, establishes a consistent framework for measuring fair value and expands disclosure for each major asset and liability category measured at fair value on either a recurring or nonrecurring basis. Fair value is defined as an exit price, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. As such, fair value is a market-based measurement that should be determined based on assumptions that market participants would use in pricing an asset or liability. As a basis for considering such assumptions, the accounting guidance establishes a three-tier fair value hierarchy, which prioritizes the inputs used in measuring fair value as follows:

Level 1: Observable inputs such as quoted prices in active markets.

Level 2: Inputs, other than the quoted prices in active markets that are observable either directly or indirectly.

Level 3: Unobservable inputs in which there is little or no market data, which require the reporting entity to develop its own assumptions.

Financial assets measured at fair value on a recurring basis consist of investment securities. Investment securities are recorded at fair value, defined as the exit price in the principal market in which we would transact, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. Level 2 securities are valued using quoted market prices for similar instruments, non-binding market prices that are corroborated by observable market data, or discounted cash flow techniques and include our investments in corporate debt securities, commercial paper, asset-backed securities and United States Treasury securities. We have no financial liabilities measured at fair value on a recurring basis. None of our non-financial assets and liabilities is recorded at fair value on a non-recurring basis. No transfers between levels have occurred during the periods presented.

Assets and liabilities measured at fair value on a recurring basis are as follows (in thousands):

		Fair Value Measurements Using		
		Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
As of December 31, 2016:				
Assets:				
Current:				
Cash equivalents	$ 29,251	$ 29,251	$ —	$ —
Available-for-sale investments, short-term:				
Commercial paper	7,843	—	7,843	—
Corporate debt securities	20,913	—	20,913	—
United States Treasury securities	5,003	5,003	—	—
Sub-total short-term investments	33,759	5,003	28,756	—
Available-for-sale investments, long-term:				
Asset-backed securities	4,002	—	4,002	—
Sub-total long-term investments	4,002	—	4,002	—
Total assets measured at fair value	$ 67,012	$ 34,254	$ 32,758	$ —
As of December 31, 2015:				
Current:				
Cash equivalents	$ 46,545	$ 46,545	$ —	$ —
Available-for-sale investments, short-term:				
Commercial paper	2,996	—	2,996	—
Corporate debt securities	39,514	—	39,514	—
Sub-total short-term investments	42,510	—	42,510	—
Available-for-sale investments, long-term:				
Asset-backed securities	10,912	—	10,912	—
Corporate debt securities	16,903	—	16,903	—
United States Treasury securities	1,999	1,999	—	—
Sub-total long-term investments	29,814	1,999	27,815	—
Total assets measured at fair value	$ 118,869	$ 48,544	$ 70,325	$ —

As of December 31, 2016 and 2015, available-for-sale investments are detailed as follows (in thousands):

	December 31, 2016			
	Gross Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Market Value
Available-for-sale investments, short-term:				
Commercial paper	$ 7,843	$ —	$ —	$ 7,843
Corporate debt securities	$ 20,942	$ —	$ (29)	$ 20,913
United States Treasury securities	5,002	1	—	5,003
	$ 33,787	$ 1	$ (29)	$ 33,759
Available-for-sale investments, long-term:				
Asset-backed securities	$ 4,001	$ 1	$ —	$ 4,002
	$ 4,001	$ 1	$ —	$ 4,002

	December 31, 2015			
	Gross Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Market Value
Available-for-sale investments, short-term:				
Commercial paper	$ 2,996	$ —	$ —	$ 2,996
Corporate debt securities	39,575	—	(61)	39,514
	$ 42,571	$ —	$ (61)	$ 42,510
Available-for-sale investments, long-term:				
Asset-backed securities	$ 10,928	$ —	$ (16)	$ 10,912
Corporate debt securities	16,990	—	(87)	16,903
United States Treasury securities	2,006	—	(7)	1,999
	$ 29,924	$ —	$ (110)	$ 29,814

Available-for-sale investments that are in an unrealized loss position as of December 31, 2016 are as follows (in thousands):

	Estimated Fair Value	Gross Unrealized Losses
Corporate debt securities	$ 20,913	$ (29)

As of December 31, 2016, all available-for-sale investments have contractual maturity dates less than one year. As of December 31, 2016, there are 11 available-for-sale investments in gross unrealized loss position, all of which have been in such position for less than twelve months.

At each reporting date, we perform an evaluation of impairment to determine if the unrealized losses are other-than-temporary. Factors considered in determining whether a loss is other-than-temporary include the length of time and extent to which fair value has been less than the cost basis, the financial condition of the issuer, and our intent and ability to hold the investment until recovery of its amortized cost basis. We intend, and have the ability, to hold our investments in unrealized loss positions until their amortized cost basis has been recovered. Based on our evaluation, we determined that the unrealized losses were not other-than-temporary as of December 31, 2016.

4. Balance Sheet Details

Property and equipment consist of the following (in thousands):

	December 31,	
	2016	2015
Computer and office equipment	$ 401	$ 336
Scientific and laboratory equipment	3,965	3,518
Tenant improvements	1,687	1,687
	6,053	5,541
Less accumulated depreciation and amortization	(4,632)	(3,748)
	$ 1,421	$ 1,793

Accrued expenses consist of the following (in thousands):

	December 31,	
	2016	2015
Accrued salaries, wages and benefits	1,977	1,710
Other accrued expenses (1)	3,473	2,885
	$ 5,450	$ 4,595

(1) Other accrued expenses include expenses for clinical research organizations and contract manufacturing organizations.

5. Debt, Commitments and Contingencies

Commercial Bank Debt

In each of July 2013 and June 2014, we borrowed $5.0 million under a $10.0 million loan and security agreement with SVB, which we refer to as the SVB Loan. Beginning in July 2014, we began to make payments of principal and interest which were due through the maturity date of June 1, 2017. The interest rate was a per annum fixed rate of 5.0% and 5.88% for the $5.0 million drawn in each of July 2013 and June 2014, respectively. The final payment was contractually due in June 2017 with an additional fee of $0.5 million. The SVB Loan was collateralized by all of our assets, other than our intellectual property, and contains customary affirmative and negative covenants, reporting requirements and events of default. In November 2016, pursuant to the loan and security agreement with Silicon Valley Bank (SVB) and Solar Capital Ltd. (Solar), we paid SVB the balance of $2.6 million, including interest and $0.5 million final payment, in full.

Term Loan

On November 18, 2016, we entered into a loan and security agreement with SVB and Solar, which we refer to as the Term Loan. SVB and Solar agreed to lend us up to $20.0 million, issuable in three separate tranches of: (i) $10.0 million which was funded on November 18, 2016; (ii) $5.0 million may be drawn down by us at any time before the earlier of June 30, 2017 or an event of default, at our discretion, subject to achievement of certain financial and clinical milestones; and (iii) $5.0 million may be drawn down by us any time after June 30, 2017 and before the earlier of December 31, 2017 or an event of default, at our discretion, subject to achievement of certain milestones specified for the second tranche and additional financial and clinical milestones.

Pursuant to the Term Loan agreement, we have interest only payments through December 1, 2017 or June 1, 2018, if we draw the second tranche, followed by consecutive equal monthly payments of principal and interest in arrears through the maturity date of November 18, 2020. The Term Loan bears interest at the prime rate, as reported in The Wall Street Journal on the last date of the month preceding the month in which interest will accrue, plus 4.10%. The Term Loan also provides for a final interest payment equal to 8.75% of the funded amount, which is due when the Term Loan becomes due or upon the prepayment of the Term Loan. We have the option to prepay the outstanding balance of the loan in full, subject to a prepayment fee ranging from 1.0% to 3.0% depending upon when the prepayment occurs, including any non-usage fees. The loan agreement provides for a 2.0% non-usage fee for any unfunded amount in the event we do not draw the second tranche and third tranche, payable no later than the expiration date for the second tranche or third tranche, as applicable, or the date of cancellation of the loan due to prepayment or an event of default.

We received cash proceeds of $7.3 million, net of a $2.6 million repayment of the principal, accrued interest and the $0.5 million final payment of the SVB Loan. We did not pay any termination or other fees in connection with the repayment of amounts due under the SVB Loan.

In connection with the Term Loan, the debt issuance costs have been recorded as a debt discount of Term Loan in our balance sheet, which are being accreted to interest expense over the life of the Term Loan using an effective interest rate of 12.28%. The final maturity payment is being accrued over the life of the Term Loan through interest expense.

Future principal payments for the Term Loan, including the final payment, are as follows (in thousands):

	December 31, 2016
2017	$ 249
2018	3,100
2019	3,348
2020	4,178
	$ 10,875

Facility Lease

In December 2011, we entered into a noncancelable operating lease that included certain tenant improvement allowances and is subject to base lease payments, which escalate over the term of the lease, additional charges for common area maintenance and other costs. The lease expires in May 2017 and we have an option to extend the lease for a period of five years. In January 2017, we extended the lease for two years to May 2019. Rent expense for the years ended December 31, 2016, 2015 and 2014 was $0.5 million, $0.4 million and $0.2 million, respectively.

In conjunction with the initial lease, we borrowed $2.0 million under a subordinated unsecured convertible promissory note issued to the venture arm of our landlord. The convertible promissory note carried an annual interest rate of 8.0%. In May 2015, the $2.0 million outstanding principal balance of the convertible promissory note and the $0.5 million accrued interest on the convertible promissory note was repaid in full in connection with our IPO.

In June 2016, we entered into a sublease agreement with a tenant of our landlord for additional facility space in our existing building that commenced in August 2016 and will expire in June 2017.

As of December 31, 2016, future minimum payments under the non-cancelable operating lease are as follows (in thousands):

	Operating Lease
2017	$ 386
2018	—
	$ 386

Research Agreements and Funding Obligations

In October 2007, we entered into a research funding and option agreement for certain technologies from The Scripps Research Institute (TSRI). Under the agreement, we provide funding to TSRI to conduct certain research activities. The agreement renews automatically for successive 12 month periods starting on May 31st of each year unless we provide 30 days' prior written notice to terminate the agreement. TSRI has the right to terminate the agreement if we fail to make any payment under the agreement or for breach or insolvency. Under the research funding and option agreement, TSRI has granted us options to enter into license agreements to acquire rights and exclusive licenses to develop, make, have made, use, have used, import, have imported, offer to sell, sell, and have sold certain licensed products, processes and services based on certain technology arising from the sponsored research activities. Pursuant to the terms of these license agreements, TSRI is entitled to receive tiered royalties as a percentage of net sales and a percentage of nonroyalty revenue we may receive from our sublicensees or partners, with the amount owed decreasing if we enter into the applicable sublicense or partnering agreement after meeting a specified clinical milestone. In addition, we are obligated to pay TSRI up to an aggregate of $2.75 million under each license agreement upon the achievement of specific clinical and regulatory milestone events. In January 2015, we and TSRI entered into an amended and restated research funding and option agreement pursuant to which we agreed to issue 119,840 shares of our common stock to TSRI in consideration for the adjustment of sublicense payments and the assignment of certain intellectual property rights by TSRI to us. The $1.4 million fair value of the common stock issued to TSRI was recorded to research and development expense. We issued the shares of common stock to TSRI on March 31, 2015. We entered into amendments to our research funding and option agreement to provide an additional $0.9 million of funding for the year ended December 31, 2016.

During the years ended December 31, 2016, 2015 and 2014, excluding the fair value of the common stock issued to TSRI described above, we recognized expense under the agreement in the amount of $1.6 million, $0.7 million and $0.6 million, respectively. A member of our board of directors is a faculty member at TSRI and such payments fund a portion of his research activities conducted at TSRI.

During the years ended December 31, 2016, 2015 and 2014, we provided charitable donations to the National Foundation for Cancer Research of $0.4 million. We have requested that the donations be restricted to certain basic research in cancer biology and therapeutics, a portion of which funds research activities conducted at TSRI in the laboratory of a member of our board of directors.

Manufacturing Agreements

On June 16, 2015, we entered into a Master Services Agreement (the MSA) with FUJIFILM Diosynth Biotechnologies U.S.A., Inc. (Fujifilm) to complete the development of the manufacturing process and for the production of the drug substance for Resolaris, our drug in clinical development. Pursuant to the MSA, Fujifilm will provide the drug substance for Resolaris to support future clinical trials, including potential pivotal trials. Under the initial scope of work executed pursuant to the MSA, Fujifilm will conduct process optimization, scale-up and demonstration, and cGMP manufacturing of the drug substance of Resolaris, and we are required to pay Fujifilm based on development and production milestones up to the mid seven figures. In addition, we are billed for consumables on a pass-through basis and have entered into statements of work for stability studies. In the next 12 months, we are committed to pay Fujifilm approximately $0.6 million based on development and production milestones. During the year ended December 31, 2016 and 2015, expenses associated with this agreement were $8.4 million and $5.1 million, respectively.

In August 2016, we entered into a Master Services Agreement with a third party contract development and manufacturing organization to complete the development of the manufacturing process and for the production of drug substance for Stalaris. We are required to pay the third party contract manufacturer a total payment in the low seven figures subject to certain rights of cancellation. In addition, we are billed for consumables on a pass-through basis. In the next 12 months, we are committed to pay the third party contract manufacturing organization approximately $2.2 million based on development and production milestones. For the year ended December 31, 2016, expenses associated with this agreement were $1.0 million.

6. Stockholders' Equity

Common Stock

In May 2015, in connection with our IPO, we filed an amended and restated certificate of incorporation, authorizing 150,000,000 shares of common stock and 7,285,456 shares of redeemable convertible preferred stock, and 5,000,000 shares of undesignated preferred stock. As of December 31, 2016, no preferred stock is issued and outstanding.

Registration Statement on Form S-3

On June 13, 2016, we filed a Registration Statement on Form S-3 (File No. 333-211998) containing two prospectuses: (i) a base prospectus which covers the offering, issuance and sale of up to $150 million in the aggregate of an indeterminate number of shares of common stock and preferred stock, an indeterminate principal amount of debt securities and such indeterminate number of warrants and units; and (ii) a sales agreement prospectus covering the offering, issuance and sale of up to a maximum aggregate offering price of up to $20 million of our common stock that may be sold from time to time under a sales agreement with Cowen and Company, LLC (Cowen). In accordance with the terms of such sales agreement entered with Cowen, we may offer and sell shares of our common stock having an aggregate offering price of up to $35 million from time to time through Cowen. We are required to file another prospectus supplement in the event we intend to offer more than $20 million in shares of our common stock in accordance with the sales agreement. The sales agreement prospectus amount of $20 million is included in the base prospectus amount of $150 million.

2014 Stock Plan

We adopted a stock option plan in 2007 (the 2007 Plan), which was subsequently amended, restated and renamed in July 2014 (the 2014 Plan) to provide for the incentive stock options, nonstatutory stock options, stock and rights to purchase restricted stock to eligible recipients. Recipients of incentive stock options are eligible to purchase shares of our common stock at an exercise price equal to no less than the estimated fair market value of such stock on the date of grant. The maximum term of options under the 2014 Plan is ten years. Options granted generally vest over four years.

2015 Stock Plan

In April 2015, our board of directors adopted, and our stockholders approved, the 2014 Stock Plan (the 2015 Plan). The 2015 Plan became effective on May 6, 2015 and we ceased granting any new awards under our 2014 Plan. Awards granted under the 2014 Plan prior to our IPO that are forfeited, canceled, reacquired by us prior to vesting satisfied without the issuance of stock or otherwise terminated (other than by exercise) will be added to shares available for issuance under the 2015 Plan. A total of 1,574,566 shares of our common stock were initially reserved for issuance under the 2015 Plan. In addition, the number of shares reserved and available for issuance under the 2015 Plan will automatically increase each January 1, beginning on January 1, 2016 and thereafter until January 1, 2019, by the lesser of (i) 1,840,000 shares, (ii) 4% of the outstanding number of shares of our common stock on the immediately preceding December 31 or (iii) an amount determined by our board of directors. Pursuant to this provision, 949,793 and 946,803 additional shares were reserved for issuance under the 2015 Plan on January 1, 2017 and 2016, respectively. Shares underlying any awards under the 2015 Plan that are forfeited, canceled, reacquired by us prior to vesting, satisfied without the issuance of stock or otherwise terminated (other than by exercise) will be added to shares available for issuance under the 2015 Plan.

The maximum term of options granted under 2015 Plan is ten years. For an initial grant to an employee, 25% of the options generally vest on the first anniversary of the original vesting date, with the balance vesting monthly over the remaining three years. For subsequent grants to an employee, the options generally vest monthly over a four-year term.

Inducement Grant

In September 2016, we granted a non-qualified option to purchase 145,000 shares of our common stock at an exercise price of $3.29 per share as an inducement award in connection with the hiring of our Senior Vice President, Research. This option will vest over a period of four (4) years, with 25% vesting on the one year anniversary of the grant date and the remaining 75% vesting on a monthly basis over three years thereafter, subject to continuous employment. This option was an inducement grant issued outside of the 2015 Plan in accordance with NASDAQ Listing Rule 5635(c)(4). We intend to file a registration statement on Form S-8 to register the shares of common stock underlying this option prior to the time at which this option becomes exercisable. In addition, from time to time, we may make inducement grants of stock options to new employees.

Employee Stock Purchase Plan

In April 2015, our board of directors adopted, and our stockholders approved, our 2015 Employee Stock Purchase Plan (the 2015 ESPP). The 2015 ESPP became effective on May 6, 2015. A total of 227,623 shares of our common stock were initially reserved for issuance under the 2015 ESPP. In addition, the number of shares reserved and available for purchase under the 2015 ESPP will automatically increase each January 1, beginning on January 1, 2016 and thereafter until January 1, 2019, by 1% of the outstanding number of shares of our common stock on the immediately preceding December 31 or such lesser number of shares as determined by the administrator of the 2015 ESPP. Pursuant to this provision, 237,448 and 236,700 additional shares were reserved for issuance under the 2015 ESPP on January 1, 2017 and 2016, respectively.

Stock-based Compensations

Stock Options

Stock option activity is summarized as follows:

	Number of Outstanding Options	Weighted Average Exercise Price	Weighted Remaining Contractual Term	Aggregate Intrinsic Value (in 000s)
Outstanding as of December 31, 2015	2,625,280	$ 8.83		
Granted	2,266,419	$ 5.56		
Exercised	(15,892)	$ 1.24		
Canceled/forfeited/expired	(860,819)	$ 10.17		
Outstanding as of December 31, 2016	4,014,988	$ 6.73	7.82	$ 519
Options vested and expected to vest as of December 31, 2016	4,014,988	$ 6.73	7.82	$ 519
Options exercisable as of December 31, 2016	1,419,562	$ 6.27	5.88	$ 519

The assumptions used in the Black-Scholes option pricing model to determine the fair value of the employee stock option grants were as follows:

	Years Ended December 31,		
	2016	2015	2014
Expected term (in years)	5.50 – 6.08	5.50 – 6.08	5.77 – 6.56
Risk-free interest rate	1.2% – 2.1%	1.5% – 1.9%	1.7% – 2.7%
Expected volatility	80.7% – 84.0%	79.2% – 100.9%	111.0%
Expected dividend yield	0.0%	0.0%	0.0%

The assumptions used in the Black-Scholes option pricing model to determine the fair value of the ESPP offering were as follows:

	December 31,	
	2016	2015
Expected term (in years)	0.50	0.50
Risk-free interest rate	0.4% – 0.6%	0.3%
Expected volatility	75.5% – 80.8%	67.3%
Expected dividend yield	0.0%	0.0%

Expected term. The expected term represents the period of time that options are expected to be outstanding. Because we do not have sufficient history of exercise behavior, we determine the expected life assumption using the simplified method, which is an average of the contractual term of the option and its vesting period.

Risk-free interest rate. We base the risk-free interest rate assumption on the U.S. Treasury's rates for U.S. Treasury zero-coupon bonds with maturities similar to those of the expected term of the award being valued.

Expected volatility. The expected volatility assumption is based on volatilities of a peer group of similar companies whose share prices are publicly available. The peer group was developed based on companies in the biotechnology industry.

Expected dividend yield. We base the expected dividend yield assumption on the fact that we have never paid cash dividends and have no present intention to pay cash dividends.

Performance Options with Market Conditions

In October 2015, we granted our employees and certain consultants performance options with a market condition to purchase up to an aggregate 169,402 shares of common stock at an exercise price of $10.24. Upon achievement of specified performance goals by October 2017, such performance-based options shall begin to vest over four years in equal monthly installments, otherwise the options will be subject to forfeiture. The fair value of the stock options awarded that include market-based performance conditions is estimated on the date of the grant using a Monte Carlo simulation, based on the market price of the underlying common stock, expected performance measurement period, expected peer group stock price volatility and expected risk-free interest rate. The weighted average grant date fair value was $4.23.The performance options with market conditions grants are expensed using the accelerated attribution method over the requisite service period of 4.8 years regardless of whether the market condition is achieved or earned and vest.

In January 2016, we granted to our executives, employees and certain consultants performance options with a market condition to purchase up to an aggregate 396,960 shares of common stock at an exercise price of $9.13. Upon achievement of specified goals by January 4, 2018, such performance options shall begin to vest over four years in equal monthly installments, otherwise the options will be subject to forfeiture. The fair value of the performance options with a market condition is estimated on the date of the grant using a Monte Carlo simulation, based on the market price of the underlying common stock, expected performance measurement period, expected peer group stock price volatility and expected risk-free interest rate. The weighted average grant date fair value was $1.93. The performance options with market conditions grants are expensed using the accelerated attribution method over the requisite service period of 5.1 years regardless of whether the market condition is achieved or earned and vest.

The assumptions used at grant date to determine the fair value of the performance options with a market condition were as follows:

	December 31,	
	2016	2015
Expected term (in years)	5.06	4.81
Risk-free interest rate	2.2%	2.1%
Expected volatility	83.3%	80.6%
Expected dividend yield	0.0%	0.0%

Restricted Stock Units

During the year ended December 31, 2016, we granted restricted stock units to employees. Restricted stock unit activity is summarized as follows:

	Number of Outstanding Restricted Stock Units	Weighted Average Grant Date Fair Value
Balance as of December 31, 2015	—	$ —
Granted	131,593	$ 4.96
Released	(2,080)	$ 5.48
Forfeited	(52,800)	$ 4.95
Balance as of December 31, 2016	76,713	$ 4.95

The allocation of stock-based compensation for all options, including performance options with market condition and restricted stock units is as follows (in thousands):

	Years Ended December 31,		
	2016	2015	2014
Research and development	$ 1,876	$ 2,524	$ 527
General and administrative	3,153	2,332	1,264
	$ 5,029	$ 4,856	$ 1,791

The weighted–average grant date fair value per share of stock options granted by us, excluding performance options with market conditions, during the years ended December 31, 2016, 2015 and 2014 was $3.34, $11.29 and $10.18, respectively. The aggregate intrinsic value of stock options exercised during the years ended December 31, 2016, 2015 and 2014 was $34,000, $1.9 million and $0.4 million, respectively. As of December 31, 2016, total unrecognized share-based compensation expense related to unvested stock options and restricted stock units was approximately $9.6 million. This unrecognized cost is expected to be recognized ratably over a weighted-average period of approximately 2.9 years.

During the fourth quarter of 2014, we modified certain vesting conditions of performance-based equity awards for our Chief Executive Officer which resulted in incremental share-based compensation costs of $0.7 million, of which $0.6 million was recognized as expense during the year ended December 31, 2014.

In October 2015, our Compensation Committee of the Board of Directors approved an amendment to accelerate the vesting schedule of certain outstanding stock options representing 931,749 shares granted to active employees and certain consultants under the 2014 Plan to change the vesting schedule of such options from six-years to four-years retroactive to the original vesting commencement dates. We recorded $0.8 million of stock compensation expense in connection with the modification during the year ended December 31, 2015.

Warrants

In November 2016, in connection with the Term Loan, we issued warrants to each of SVB and Solar to purchase an aggregate of 47,771 shares of our common stock with an exercise price of $3.14 per share. The warrants are immediately exercisable and will expire on November 18, 2023, provided that such warrants have not been previously exercised or have expired in connection with certain fundamental transactions involving us.

Warrants outstanding as of December 31, 2016:

Number Outstanding	Exercise Price Per Share	Expiration Date
9,051	$ 6.63	September 2017
2,006	$ 7.48	March 2021
14,913	$ 20.12	July 2023
95,542	$ 3.14	November 2023
121,512		

Common Stock Reserved for Future Issuance

Common stock reserved for future issuance is as follows:

	As of December 31,	
	2016	2015
Common stock warrants	121,512	25,970
Common stock options and awards outstanding	4,091,701	2,625,280
Shares available under the 2015 Plan	510,760	903,350
Shares available under the 2015 ESPP Plan	407,542	227,623
	5,131,515	3,782,223

7. Income Taxes

Pretax earnings (loss) were generated by both domestic and foreign operations as follows (in thousands):

	Years Ended December 31,		
	2016	2015	2014
United States	$ (57,096)	$ (47,490)	$ (34,885)
Foreign	(808)	(483)	10,535
	$ (57,904)	$ (47,973)	$ (24,350)

A reconciliation of the expected statutory federal income tax provision to the actual income tax provision is summarized as follows (in thousands):

	Years Ended December 31,		
	2016	2015	2014
Expected income taxes benefit at federal statutory rate	$ (19,687)	$ (16,311)	$ (8,279)
State income taxes, net of federal benefit	—	—	(2,023)
Permanent items and other	675	865	368
Research credits	(6,800)	(2,674)	(372)
Unrecognized tax benefits	2,720	1,070	144
Foreign rate differential	141	84	(3,391)
Change in tax rate	—	3,551	—
Change in valuation allowance	22,902	13,415	13,553
Income tax (benefit) expense	$ (49)	$ —	$ —

Deferred income taxes are provided for temporary differences in recognizing certain income and expense items for financial and tax reporting purposes. The deferred tax assets consisted primarily of the income tax benefits from net operating loss (NOL) carryforwards, research and development credits and capitalized research and development expenses, along with other accruals and reserves. Valuation allowances of $71.2 million and $48.3 million as of December 31, 2016 and 2015, respectively, have been recorded to offset deferred tax assets as realization of such assets does not meet the more-likely-than-not threshold under ASC 740, *Accounting for Income Taxes*.

Significant components of our deferred tax assets are summarized as follows (in thousands):

	December 31,	
	2016	2015
Net operating loss carryforwards	$ 33,713	$ 24,869
Capitalized research and development expenses	21,624	14,181
Research credits and other state credits	9,227	3,565
Intangible assets	3,874	4,176
Reserve and accruals	2,711	1,528
Valuation allowance	(71,149)	(48,319)
Net deferred tax assets	$ —	$ —

As of December 31, 2016, we had approximately $87.8 million, $94.5 million, and $6.5 million of net operating loss carryforwards for federal, state, and foreign purposes, respectively, net of Section 382 limitations, available to offset future taxable income. The federal and state net operating loss carryforwards begin to expire in 2025 and 2016, respectively. California net operating loss carryforwards of $1.4 million will expire in 2017. California net operating loss carryforwards of $93.1 million will expire from 2028 through 2034. The foreign net operating losses carry over indefinitely. As of December 31, 2016, we had federal and state research and development credit carryforwards of approximately $2.8 million and $2.5 million, respectively, net of Section 382 limitations, which begin to expire in 2026 for federal purposes and carry over indefinitely for state purposes. We had $11.0 million of federal Orphan Drug Credits as of December 31, 2016, which will begin to expire in 2035.

In November 2015, the FASB issued ASU No. 2015-17, *Balance Sheet Classification of Deferred Taxes,* which requires all deferred tax assets and liabilities to be classified as noncurrent on the balance sheet. The new accounting guidance is effective for annual reporting periods beginning after December 15, 2016 and interim periods therein. Early adoption is permitted as of the beginning of interim or annual reporting periods. We elected to early adopt this guidance prospectively beginning in the year ended December 31, 2015 and prior periods were not retrospectively adjusted. There was no material impact on the consolidated financial position or results of operations upon adoption.

Utilization of the domestic NOL and research and development credit carryforwards may be subject to a substantial annual limitation due to ownership change limitations that may have occurred or that could occur in the future, as required by Section 382 and 383 of the Internal Revenue Code of 1986, as amended (the Code), as well as similar state and foreign provisions. These ownership changes may limit the amount of NOL and research and development credit carryforwards 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 of the outstanding stock of a company by certain stockholders. Since the Company’s formation, we raised capital through the issuance of capital stock on several occasions which on its own or combined with the purchasing stockholders’ subsequent disposition of those shares, has resulted in such an ownership change, and could result in an ownership change in the future.

Upon the occurrence of an ownership change under Section 382 as outlined above, utilization of the NOL and research and development credit carryforwards become subject to an annual limitation under Section 382 of the Code, which is determined by first multiplying the value of our stock at the time of the ownership change by the applicable long-term, tax-exempt rate, which could be subject to additional adjustments. Any limitation may result in expiration of a portion of the NOL or research and development credit carryforwards before utilization. We completed an analysis through September 7, 2011, and had adjusted our NOL and research and development tax credit carryforwards accordingly. Ownership changes that may have occurred subsequent to September 7, 2011, and future ownership changes, including any ownership change resulting from this offering, may further limit our ability to utilize its remaining tax attributes.

We recognize a tax benefit from an uncertain tax position when it is more likely than not that the position will be sustained upon examination, including resolutions of any related appeals or litigation processes, based on the technical merits. Income tax positions must meet a more-likely-than-not recognition threshold to be recognized.

Our practice is to recognize interest and penalties related to income tax matters in income tax expense. We had no accrual for interest and penalties on our balance sheet and had not recognized interest or penalties in the consolidated statements of operations for the years ended December 31, 2016, 2015 and 2014.

Due to the existence of the valuation allowance, future changes in unrecognized tax benefits will not impact our effective tax rate.

Uncertain tax positions are evaluated based upon the facts and circumstances that exist at each reporting period. Subsequent changes in judgment based upon new information may lead to changes in recognition, derecognition, and measurement. Adjustments may result, for example, upon resolution of an issue with the taxing authorities, or expiration of a statute of limitations barring an assessment for an issue.

The activity related to our unrecognized tax benefits is summarized as follows (in thousands):

	December 31,		
	2016	2015	2014
Balance as of beginning of year	$ 5,033	$ 1,106	$ 947
Increase related to prior year tax positions	1,890	2,404	—
Increase related to current year tax positions	6,077	1,523	177
Other decreases	—	—	(18)
Balance as of end of year	$ 13,000	$ 5,033	$ 1,106

We do not anticipate that the amount of unrecognized tax benefits as of December 31, 2016 will change within the next twelve months.

We are subject to taxation in the United States, Hong Kong and state jurisdictions. Our tax years from inception are subject to examination by the United States, Hong Kong and California authorities due to the carry forward of unutilized NOLs and research and development credits.

8. Employee Benefits

401(k) Plan

We maintain a defined contribution 401(k) plan available to eligible employees. Employee contributions are voluntary and are determined on an individual basis, limited to the maximum amount allowable under federal tax regulations. In April 2015, our Board of Directors approved a policy, beginning on June 1, 2015, to match employee contributions equal to 50% of the participant's contribution of up to a maximum of 6% of the participant's annual salary. We made discretionary contributions totaling $0.2 million and $0.1 million during the years ended December 31, 2016 and 2015, respectively.

9. Quarterly Financial Data (Unaudited)

The following financial information reflects all normal recurring adjustments, which are, in our opinion, necessary for a fair statement of the results of the interim periods. Summarized quarterly data for 2016 and 2015 are as follows (in thousands, except per share data):

	For the quarters ended			
	March 31	June 30	September 30	December 31
2016:				
Operating expenses	$ 16,115	$ 15,433	$ 13,865	$ 12,527
Net loss	(16,087)	(15,383)	(13,819)	(12,566)
Basic and diluted net loss per share	$ (0.68)	$ (0.65)	$ (0.58)	(0.53)
2015:				
Operating expenses	$ 8,922	$ 10,898	$ 11,313	$ 16,483
Net loss	(9,071)	(11,080)	(11,329)	(16,493)
Basic and diluted net loss per share	$ (9.39)	$ (0.74)	$ (0.48)	(0.70)

Net loss per share is computed independently for each of the quarters presented. Therefore, the sum of the quarterly per-share calculations will not necessarily equal the annual per share calculation.

10. Subsequent Events

In January 2017, we extended our primary facility lease with our landlord through May 2019 for an additional commitment of $1.5 million.

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

We maintain disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, or the Exchange Act, that are designed to ensure that information required to be disclosed in our periodic and current reports that we file with the SEC is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to our management, including our Principal Executive Officer and Principal Financial Officer, as appropriate, to allow timely decisions regarding required disclosure. In designing and evaluating the disclosure controls and procedures, management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable and not absolute assurance of achieving the desired control objectives. In reaching a reasonable level of assurance, management necessarily is required to apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures. In addition, the design of any system of controls also is based in part upon certain assumptions about the likelihood of future events, and there can be no assurance that any design will succeed in achieving its stated goals under all potential future conditions; over time, control may become inadequate because of changes in conditions, or the degree of compliance with policies or procedures may deteriorate. Because of the inherent limitations in a cost-effective control system, misstatements due to error or fraud may occur and not be detected.

We carried out an evaluation, under the supervision and with the participation of our management, including our Principal Executive Officer and Principal Financial Officer, of the effectiveness of the design and operation of our disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the Exchange Act. Based on this evaluation, our Principal Executive Officer and Principal Financial Officer concluded that our disclosure controls and procedures were effective at the reasonable assurance level as of December 31, 2016.

Management's Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting as such term is defined in Rules 13a-15(f) and 15-d-15(f) of the Exchange Act. Internal control over financial reporting is a process designed under the supervision and with the participation of our management, including our Principal Executive Officer and Principal Financial Officer, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with accounting principles generally accepted in the United States of America.

As of December 31, 2016, our management assessed the effectiveness of our internal control over financial reporting using the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission in Internal Control – 2013 Integrated Framework (2013 Framework). Based on this assessment, our management concluded that our internal control over financial reporting was effective as of December 31, 2016.

This Annual Report on Form 10-K does not include an attestation report of our registered public accounting firm due to a transition period established by the JOBS Act for emerging growth companies.

Changes in Internal Control Over Financial Reporting

During the quarter ended December 31, 2016, there have been no changes in our internal control over financial reporting, as such term is defined in Rules 13a-15(f) and 15d-15(f) promulgated under the Exchange Act, that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance

Except as set forth below, the information required by this item will be contained in our 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, or Proxy Statement, and is incorporated herein by reference.

We have adopted a written code of ethics for directors, officers (including our principal executive officer, principal financial officer and principal accounting officer or persons performing similar functions) and employees, known as the Code of Business Conduct and Ethics. The Code of Business Conduct and Ethics is available on our website at *http://www.atyrpharma.com* under the Corporate Governance section of our Investors page. If we make any substantive amendments to, or grant any waivers from, the Code of Business Conduct and Ethics for any officer or director, we will disclose the nature of such amendment or waiver on our website or in a Current Report on Form 8-K.

Item 11. Executive Compensation

The information required by this item will be contained in our Proxy Statement and is incorporated herein by reference.

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

The information required by this item will be contained in our Proxy Statement and is incorporated herein by reference.

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

The information required by this item will be contained in our Proxy Statement and is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services

The information required by this item will be contained in our Proxy Statement and is incorporated herein by reference.

PART IV

Item 15. Exhibits and Financial Statement Schedules

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

1. *Index list to Financial Statements*:

2. *Financial Statement Schedules.*

Schedules have been omitted as all required information has been disclosed in the financial statements and related footnotes.

3. *Exhibits.*

The Exhibits listed in the Exhibit Index are filed as a part of this Form 10-K.

Item 16. Form 10-K Summary

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this Annual Report on Form 10-K to be signed on its behalf by the undersigned, thereunto duly authorized.

aTyr Pharma, Inc.

Date: March 16, 2017

By /s/ John D. Mendlein
John D. Mendlein, Ph.D.
Chief Executive Officer
(Principal Executive Officer)

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints John D. Mendlein and John T. Blake, jointly and severally, and each of them, his or her true and lawful attorneys-in-fact, each with full power of substitution, for him or her in any and all capacities, to sign any 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 each of said attorneys-in-fact or their substitute or substitutes may do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this Annual Report on Form 10-K has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ John D. Mendlein John D. Mendlein, Ph.D.	Chief Executive Officer and Director, (Principal Executive Officer)	March 16, 2017
/s/ John T. Blake John T. Blake	Senior Vice President, Finance (Principal Financial and Accounting Officer)	March 16, 2017
/s/ John K. Clarke John K. Clarke	Chairman of the Board	March 16, 2017
/s/ Srinivas Akkaraju Srinivas Akkaraju, M.D., Ph.D.	Director	March 16, 2017
/s/ James C. Blair James C. Blair, Ph.D.	Director	March 16, 2017
/s/ Kathryn E. Falberg Kathryn E. Falberg	Director	March 16, 2017
/s/ Mark Goldberg Mark Goldberg, M.D.	Director	March 16, 2017
/s/ Amir H. Nashat Amir H. Nashat, Sc.D.	Director	March 16, 2017
/s/ Paul Schimmel Paul Schimmel, Ph.D.	Director	March 16, 2017

EXHIBIT INDEX

Exhibit Number	Exhibit Title	Incorporated by Reference			Filing Date
		Form	File No.	Exhibit	
3.1	Restated Certificate of Incorporation of the Registrant	S-1/A	333-203272	3.2	May 1, 2015
3.2	Amended and Restated Bylaws of the Registrant	S-1/A	333-203272	3.4	April 27, 2015
4.1	Specimen Common Stock Certificate	S-1/A	333-203272	4.1	April 27, 2015
4.2	Warrant to Purchase Stock issued to Comerica Bank on September 18, 2007	S-1	333-203272	4.2	April 6, 2015
4.3	Warrant to Purchase Stock issued to Comerica Bank on March 18, 2011	S-1	333-203272	4.3	April 6, 2015
4.4	Warrant to Purchase Stock issued to Silicon Valley Bank on July 24, 2013	S-1	333-203272	4.4	April 6, 2015
4.5	Warrant to Purchase Stock issued to Silicon Valley Bank on November 18, 2016	—	—	—	Filed herewith
4.6	Warrant to Purchase Stock issued to Solar Capital Ltd on November 18, 2016	—	—	—	Filed herewith
10.1#	2014 Stock Plan and forms of agreements thereunder	S-1/A	333-203272	10.1	April 27, 2015
10.2#	2015 Stock Option and Incentive Plan and forms of agreements thereunder	S-1/A	333-203272	10.2	April 27, 2015
10.3#	Amended and Restated Employment Agreement by and between the Registrant and John D. Mendlein, Ph.D., dated as of December 23, 2015	10-K	001-37378	10.3	March 30, 2016
10.4#	Amended and Restated Restricted Stock Purchase Agreement by and between the Registrant and John D. Mendlein, Ph.D., dated as of December 18, 2014	S-1	333-203272	10.6	April 6, 2015
10.5†	Amended and Restated Research Funding and Option Agreement by and between the Registrant and The Scripps Research Institute, dated January 19, 2015	S-1	333-203272	10.7	April 6, 2015
10.6	Master Services Agreement by and between the Registrant and Syngene International Limited, dated November 5, 2012	S-1	333-203272	10.8	April 6, 2015
10.7	Lease by and between the Registrant and BMR-John Hopkins Court LLC, dated December 22, 2011	S-1	333-203272	10.9	April 6, 2015
10.8	First Amendment to Lease between the Registrant and BMR-3545-3575 JOHN HOPKINS LP (as successor-in-interest to BMR-John Hopkins Court LLC), dated January 4, 2016	—	—	—	Filed herewith
10.9	Registration and Voting Rights Agreement by and among the Registrant and the stockholders named therein, dated March 31, 2015	S-1/A	333-203272	10.11	April 27, 2015
10.10	Form of Indemnification Agreement entered into between the Registrant and its directors	S-1/A	333-203272	10.12	April 27, 2015
10.11	Form of Indemnification Agreement entered into between the Registrant and its officers	S-1/A	333-203272	10.13	April 27, 2015
10.12#	2015 Employee Stock Purchase Plan	S-1/A	333-203272	10.14	April 27, 2015

Exhibit Number	Exhibit Title	Incorporated by Reference			
		Form	File No.	Exhibit	Filing Date
10.13†	Master Services Agreement by and between the Registrant and Fujifilm Diosynth Biotechnologies U.S.A., Inc., dated June 16, 2015	10-Q/A	001-37378	10.1	November 25, 2015
10.14#	Senior Executive Cash Incentive Bonus Plan	8-K	001-37378	10.1	January 29, 2016
10.15#	Executive Severance and Change in Control Policy	10-K	001-37378	10.6	March 30, 2016
10.16#	Registrant's Non-Qualified Stock Option Agreement for Non-Plan Inducement Grant	10-Q	001-37378	10.1	November 14, 2016
10.17†	Loan and Security Agreement by and between the Registrant and Silicon Valley Bank and Solar Capital Ltd, dated November 18, 2016	—	—	—	Filed herewith
10.18#	Employment Offer Letter by and between the Registrant and Sanuj K. Ravindran, M.D., dated October 23, 2015	—	—	—	Filed herewith
10.19#	Employment Offer Letter by and between the Registrant and Sanjay S. Shukla, M.D., M.S., dated March 30, 2016	—	—	—	Filed herewith
14.1	Code of Business Conduct and Ethics	10-Q	001-37378	14.1	June 18, 2015
21.1	Subsidiaries of the Registrant	S-1	333-203272	21.1	April 6, 2015
23.1	Consent of Independent Registered Public Accounting Firm	—	—	—	Filed herewith
24.1	Power of Attorney (included on signature page to this Annual Report)	—	—	—	Filed herewith
31.1	Certification of Principal 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.	—	—	—	Filed herewith
31.2	Certification of Principal 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.	—	—	—	Filed herewith
32.1	Certification of Principal Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.	—	—	—	Filed herewith
32.2	Certification of Principal Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.	—	—	—	Filed herewith
101.INS	XBRL Instance Document	—	—	—	Filed herewith
101.SCH	XBRL Taxonomy Extension Schema Document	—	—	—	Filed herewith
101.CAL	XBRL Taxonomy Extension Calculation Linkbase Document	—	—	—	Filed herewith
101.DEF	XBRL Taxonomy Extension Definition Linkbase Document	—	—	—	Filed herewith
101.LAB	XBRL Taxonomy Extension Label Linkbase Document	—	—	—	Filed herewith
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document	—	—	—	Filed herewith

# Indicates a management contract or compensatory plan, contract or arrangement.

† Application has been made to the Securities and Exchange Commission for confidential treatment of certain provisions. Omitted material for which confidential treatment has been requested has been filed separately with the Securities and Exchange Commission.

Exhibit 4.5

THIS WARRANT AND THE SHARES ISSUABLE HEREUNDER HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE "ACT"), OR THE SECURITIES LAWS OF ANY STATE AND, EXCEPT AS SET FORTH IN SECTIONS 5.3 AND 5.4 BELOW, MAY NOT BE OFFERED, SOLD, PLEDGED OR OTHERWISE TRANSFERRED UNLESS AND UNTIL REGISTERED UNDER SAID ACT AND LAWS OR IN FORM AND SUBSTANCE SATISFACTORY TO THE COMPANY, SUCH OFFER, SALE, PLEDGE OR OTHER TRANSFER IS EXEMPT FROM SUCH REGISTRATION.

WARRANT TO PURCHASE COMMON STOCK

Company: ATYR PHARMA, INC.
Number of Shares of Common Stock: 47,771
Warrant Price: $3.14
Issue Date: November 18, 2016
Expiration Date: November 18, 2023 **See also Section 5.1(b).**
Credit Facility: This Warrant to Purchase Common Stock ("**Warrant**") is issued in connection with that certain Loan and Security Agreement of even date herewith between Silicon Valley Bank and the Company (the "**Loan Agreement**").

THIS WARRANT CERTIFIES THAT, for good and valuable consideration, SILICON VALLEY BANK (together with any successor or permitted assignee or transferee of this Warrant or of any shares issued upon exercise hereof, "**Holder**") is entitled to purchase the number of fully paid and non-assessable shares (the "**Shares**") of the above-stated common stock (the "**Common Stock**") of the above-named company (the "**Company**") at the above-stated Warrant Price, all as set forth above and as adjusted pursuant to Section 2 of this Warrant, subject to the provisions and upon the terms and conditions set forth in this Warrant. Reference is made to Section 5.4 of this Warrant whereby Silicon Valley Bank shall transfer this Warrant to its parent company, SVB Financial Group.

SECTION 1. EXERCISE.

1.1 Method of Exercise. Holder may at any time and from time to time through 5:00 PM Pacific Time on the Expiration Date exercise this Warrant, in whole or in part, by delivering to the Company the original of this Warrant together with a duly executed Notice of Exercise in substantially the form attached hereto as Appendix 1 and, unless Holder is exercising this Warrant pursuant to a cashless exercise set forth in Section 1.2, a check, wire transfer of same-day funds (to an account designated by the Company), or other form of payment acceptable to the Company for the aggregate Warrant Price for the Shares being purchased.

1.2 Cashless Exercise. On any exercise of this Warrant, in lieu of payment of the aggregate Warrant Price in the manner as specified in Section 1.1 above, but otherwise in accordance with the requirements of Section 1.1, Holder may elect to receive Shares equal to the value of this Warrant, or portion hereof as to which this Warrant is being exercised as set forth in the following sentence. Thereupon, the Company shall issue to the Holder such number of fully paid and non-assessable Shares as are computed using the following formula:

$$X = Y(A-B)/A$$

where:

X = the number of Shares to be issued to the Holder;

Y = the number of Shares with respect to which this Warrant is being exercised (inclusive of the Shares surrendered to the Company in payment of the aggregate Warrant Price);

A = the Fair Market Value (as determined pursuant to Section 1.3 below) of one Share; and

B = the Warrant Price.

1.3 Fair Market Value. If the Company's Common Stock is then traded or quoted on a nationally recognized securities exchange, inter-dealer quotation system or over-the-counter market (a "**Trading Market**"), the fair market value of a Share shall be the closing price or last sale price of a share of Common Stock reported for the Business Day immediately before the date on which Holder delivers this Warrant together with its Notice of Exercise to the Company. If the Company's Common Stock is not traded in a Trading Market, the Board of Directors of the Company shall determine the fair market value of a Share in its reasonable good faith judgment.

1.4 Delivery of Certificate and New Warrant. Within a reasonable time after Holder exercises this Warrant in the manner set forth in Section 1.1 or 1.2 above, the Company shall deliver to Holder a certificate representing the Shares issued to Holder upon such exercise and, if this Warrant has not been fully exercised and has not expired, a new warrant of like tenor representing the Shares not so acquired.

1.5 Replacement of Warrant. On receipt of evidence reasonably satisfactory to the Company of the loss, theft, destruction or mutilation of this Warrant and, in the case of loss, theft or destruction, on delivery of an indemnity agreement reasonably satisfactory in form, substance and amount to the Company or, in the case of mutilation, on surrender of this Warrant to the Company for cancellation, the Company shall, within a reasonable time, execute and deliver to Holder, in lieu of this Warrant, a new warrant of like tenor and amount.

1.6 Treatment of Warrant Upon Acquisition of Company.

(a) Acquisition. For the purpose of this Warrant, "**Acquisition**" means any transaction or series of related transactions involving: (i) the sale, lease, exclusive license, or other disposition of all or substantially all of the assets of the Company (ii) any merger or consolidation of the Company into or with another person or entity (other than a merger or consolidation effected exclusively to change the Company's domicile), or any other corporate reorganization, in which the stockholders of the Company in their capacity as such immediately prior to such merger, consolidation or reorganization, own less than a majority of the Company's (or the surviving or successor entity's) outstanding voting power immediately after such merger, consolidation or reorganization; or (iii) any sale or other transfer by the stockholders of the Company of shares representing at least a majority of the Company's then-total outstanding combined voting power.

(b) Treatment of Warrant at Acquisition. In the event of an Acquisition in which the consideration to be received by the Company's stockholders consists solely of cash, solely of Marketable Securities or a combination of cash and Marketable Securities (a "**Cash/Public Acquisition**"), and the fair market value of one Share as determined in accordance with Section 1.3 above would be greater than the Warrant Price in effect on such date immediately prior to such Cash/Public Acquisition, and Holder has not exercised this Warrant pursuant to Section 1.1 above as to all Shares, then this Warrant shall automatically be deemed to be Cashless Exercised pursuant to Section 1.2 above as to all Shares effective immediately prior to and contingent upon the consummation of a Cash/Public Acquisition. In connection with such Cashless Exercise, Holder shall be deemed to have restated each of the representations and warranties in Section 4 of the Warrant as the date thereof and the Company shall promptly notify the Holder of the number of Shares (or such other securities) issued upon exercise. In the event of a Cash/Public Acquisition where the fair market value of one Share as determined in accordance with Section 1.3 above would be less than the Warrant Price in effect immediately prior to such Cash/Public Acquisition, then this Warrant will expire immediately prior to the consummation of such Cash/Public Acquisition.

(c) Upon the closing of any Acquisition other than a Cash/Public Acquisition defined above, the acquiring, surviving or successor entity shall assume the obligations of this Warrant, and this Warrant shall thereafter be exercisable for the same securities and/or other property as would have been paid for the Shares issuable upon exercise of the unexercised portion of this Warrant as if such Shares were outstanding on and as of the closing of such Acquisition, subject to further adjustment from time to time in accordance with the provisions of this Warrant.

(d) As used in this Warrant, "**Marketable Securities**" means securities meeting all of the following requirements: (i) the issuer thereof is then subject to the reporting requirements of Section 13 or Section 15(d) of the Securities Exchange Act of 1934, as amended (the "**Exchange Act**"), and is then current in its filing of all required reports and other information under the Act and the Exchange Act; (ii) the class and series of shares or other security of the issuer that would be received by Holder in connection with the Acquisition were Holder to exercise this Warrant on or prior to the closing thereof is then traded in a Trading Market, and (iii) following the closing of such Acquisition, Holder would not be restricted from publicly re-selling all of the issuer's shares and/or other securities that would be received by Holder in such Acquisition were Holder to exercise or convert this Warrant in full on or prior to the closing of such Acquisition, except to the extent that any such restriction (x) arises solely under federal or state securities laws, rules or regulations, and (y) does not extend beyond six (6) months from the closing of such Acquisition.

SECTION 2. ADJUSTMENTS TO THE SHARES AND WARRANT PRICE.

2.1 Stock Dividends, Splits, Etc. If the Company declares or pays a dividend or distribution on the outstanding shares of the Common Stock payable in securities or property (other than cash), then upon exercise of this Warrant, for each Share acquired, Holder shall receive, without additional cost to Holder, the total number and kind of securities and property which Holder would have received had Holder owned the Shares of record as of the date the dividend or distribution occurred. If the Company subdivides the outstanding shares of the Common Stock by reclassification or otherwise into a greater number of shares, the number of Shares purchasable hereunder shall be proportionately increased and the Warrant Price shall be proportionately decreased. If the outstanding shares of the Common Stock are combined or consolidated, by reclassification or otherwise, into a lesser number of shares, the Warrant Price shall be proportionately increased and the number of Shares shall be proportionately decreased.

2.2 Reclassification, Exchange, Combinations or Substitution. Upon any event whereby all of the outstanding shares of the Common Stock are reclassified, exchanged, combined, substituted, or replaced for, into, with or by Company securities of a different class and/or series, then from and after the consummation of such event, this Warrant will be exercisable for the number, class and series of Company securities that Holder would have received had the Shares been outstanding on and as of the consummation of such event, and subject to further adjustment thereafter from time to time in accordance with the provisions of this Warrant. The provisions of this Section 2.2 shall similarly apply to successive reclassifications, exchanges, combinations substitutions, replacements or other similar events.

2.3 Intentionally Omitted.

2.4 Intentionally Omitted.

2.5 No Fractional Share. No fractional Share shall be issuable upon exercise of this Warrant and the number of Shares to be issued shall be rounded down to the nearest whole Share. If a fractional Share interest arises upon any exercise of the Warrant, the Company shall eliminate such fractional Share interest by paying Holder in cash the amount computed by multiplying the fractional interest by (i) the fair market value (as determined in accordance with Section 1.3 above) of a full Share, less (ii) the then-effective Warrant Price.

2.6 Notice/Certificate as to Adjustments. Upon each adjustment of the Warrant Price, Common Stock and/or number of Shares, the Company, at the Company's expense, shall notify Holder in writing within a reasonable time setting forth the adjustments to the Warrant Price, class and/or number of Shares and facts upon which such adjustment is based. The Company shall, upon written request from Holder, furnish Holder with a certificate of its Chief Financial Officer, including computations of such adjustment and the Warrant Price, class and number of Shares in effect upon the date of such adjustment.

SECTION 3. REPRESENTATIONS AND COVENANTS OF THE COMPANY.

3.1 Representations and Warranties. The Company represents and warrants to, and agrees with, the Holder as follows:

(a) The initial Warrant Price referenced on the first page of this Warrant is not greater than the price per share at which shares of Company Common Stock or options to purchase shares of Company Common Stock were issued immediately prior to the Issue Date hereof.

(b) All Shares which may be issued upon the exercise of this Warrant, shall, upon issuance, be duly authorized, validly issued, fully paid and non-assessable, and free of any liens and encumbrances except for restrictions on transfer provided for herein or under applicable federal and state securities laws. The Company covenants that it shall at all times cause to be reserved and kept available out of its authorized and unissued capital stock such number of securities as will be sufficient to permit the exercise in full of this Warrant.

3.2 Notice of Certain Events. If the Company proposes at any time to:

(a) declare any dividend or distribution upon the outstanding shares of the Company's stock, whether in cash, property, stock, or other securities and whether or not a regular cash dividend;

(b) offer for subscription or sale pro rata to the holders of the outstanding shares any additional shares of any class or series of the Company's stock (other than pursuant to contractual pre-emptive rights);

(c) effect any reclassification, exchange, combination, substitution, reorganization or recapitalization of the outstanding shares of the Common Stock; or

(d) effect an Acquisition or to liquidate, dissolve or wind up;

then, in connection with each such event, the Company shall give Holder:

(1) in the case of the matters referred to in (a) and (b) above, at least seven (7) Business Days prior written notice of the earlier to occur of the effective date thereof or the date on which a record will be taken for such dividend, distribution, or subscription rights (and specifying the date on which the holders of outstanding shares of the Common Stock will be entitled thereto) or for determining rights to vote, if any, and

(2) in the case of the matters referred to in (c) and (d) above at least seven (7) Business Days prior written notice of the date when the same will take place (and specifying the date on which the holders of outstanding shares of the Class will be entitled to exchange their shares for the securities or other property deliverable upon the occurrence of such event and such reasonable information as Holder may reasonably require regarding the treatment of this Warrant in connection with such event giving rise to the notice).

Company will also provide information requested by Holder that is reasonably necessary to enable Holder to comply with Holder's accounting or reporting requirements.

SECTION 4. REPRESENTATIONS, WARRANTIES OF THE HOLDER.

The Holder represents and warrants to the Company as follows:

4.1 Purchase for Own Account. This Warrant and the Shares to be acquired upon exercise of this Warrant by Holder are being acquired for investment for Holder's account, not as a nominee or agent, and not with a view to the public resale or distribution within the meaning of the Act. Holder also represents that it has not been formed for the specific purpose of acquiring this Warrant or the Shares.

4.2 Disclosure of Information. Holder is aware of the Company's business affairs and financial condition and has received or has had full access to all the information it considers necessary or appropriate to make an informed investment decision with respect to the acquisition of this Warrant and its underlying securities. Holder further has had an opportunity to ask questions and receive answers from the Company regarding the terms and conditions of the offering of this Warrant and its underlying securities and to obtain additional information (to the extent the Company possessed such information or could acquire it without unreasonable effort or expense) necessary to verify any information furnished to Holder or to which Holder has access.

4.3 Investment Experience. Holder understands that the purchase of this Warrant and its underlying securities involves substantial risk. Holder has experience as an investor in securities of companies in the development stage and acknowledges that Holder can bear the economic risk of such Holder's investment in this Warrant and its underlying securities and has such knowledge and experience in financial or business matters that Holder is capable of evaluating the merits and risks of its investment in this Warrant and its underlying securities and/or has a preexisting personal or business relationship with the Company and certain of its officers, directors or controlling persons of a nature and duration that enables Holder to be aware of the character, business acumen and financial circumstances of such persons.

4.4 Accredited Investor Status. Holder is an "accredited investor" within the meaning of Regulation D promulgated under the Act.

4.5 The Act. Holder understands that this Warrant and the Shares issuable upon exercise hereof have not been registered under the Act in reliance upon a specific exemption therefrom, which exemption depends upon, among other things, the bona fide nature of the Holder's investment intent as expressed herein. Holder understands that this Warrant and the Shares issued upon any exercise hereof must be held indefinitely unless subsequently registered under the Act and qualified under applicable state securities laws, or unless exemption from such registration and qualification are otherwise available. Holder is aware of the provisions of Rule 144 promulgated under the Act.

4.6 No Voting Rights. Holder, as a Holder of this Warrant, will not have any voting rights or other rights as a stockholder until the exercise of this Warrant.

SECTION 5. MISCELLANEOUS.

5.1 Term and Automatic Conversion Upon Expiration.

(a) Term. Subject to the provisions of Section 1.6 above, this Warrant is exercisable in whole or in part at any time and from time to time on or before 6:00 PM, Pacific time, on the Expiration Date and shall be void thereafter.

(b) Automatic Cashless Exercise upon Expiration. In the event that, upon the Expiration Date, the fair market value of one Share (or other security issuable upon the exercise hereof) as determined in accordance with Section 1.3 above is greater than the Warrant Price in effect on such date, then this Warrant shall automatically be deemed on and as of such date to be exercised pursuant to Section 1.2 above as to all Shares (or such other securities) for which it shall not previously have been exercised, and the Company shall, within a reasonable time, cause its transfer agent and registrar to register in book-entry format or to deliver to Holder a certificate representing the Shares (or such other securities) issued upon such exercise to Holder.

5.2 Legends. The Shares shall be imprinted with a legend in substantially the following form:

> THE SHARES EVIDENCED BY THIS CERTIFICATE HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE "**ACT**"), OR THE SECURITIES LAWS OF ANY STATE AND, EXCEPT AS SET FORTH IN THAT CERTAIN WARRANT TO PURCHASE COMMON STOCK ISSUED BY THE ISSUER TO SILICON VALLEY BANK DATED OCTOBER __, 2016, MAY NOT BE OFFERED, SOLD, PLEDGED OR OTHERWISE TRANSFERRED UNLESS AND UNTIL REGISTERED UNDER SAID ACT AND LAWS OR IN FORM AND SUBSTANCE SATISFACTORY TO THE ISSUER, SUCH OFFER, SALE, PLEDGE OR OTHER TRANSFER IS EXEMPT FROM SUCH REGISTRATION.

5.3 Compliance with Securities Laws on Transfer. This Warrant and the Shares issuable upon exercise of this Warrant may not be transferred or assigned in whole or in part except in compliance with applicable federal and state securities laws by the transferor and the transferee (including, without limitation, the delivery of investment representation letters and legal opinions reasonably satisfactory to the Company, as reasonably requested by the Company). The Company shall not require Holder to provide an opinion of counsel if the transfer is to SVB Financial Group (Silicon Valley Bank's parent company) or any other affiliate of Holder, provided that any such transferee is an "accredited investor" as defined in Regulation D promulgated under the Act. Additionally, the Company shall also not require an opinion of counsel if there is no material question as to the availability of Rule 144 promulgated under the Act.

5.4 Transfer Procedure. After receipt by Silicon Valley Bank of the executed Warrant, Silicon Valley Bank will transfer all of this Warrant to its parent company, SVB Financial Group. By its acceptance of this Warrant, SVB Financial Group hereby makes to the Company each of the representations and warranties set forth in Section 4 hereof and agrees to be bound by all of the terms and conditions of this Warrant as if the original Holder hereof. Subject to the provisions of Section 5.3 and upon providing the Company with written notice, SVB Financial Group and any subsequent Holder may transfer all or part of this Warrant or the Shares issuable upon exercise of this Warrant to any transferee, provided, however, in connection with any such transfer, SVB Financial Group or any subsequent Holder will give the Company notice of the portion of the Warrant being transferred with the name, address and taxpayer identification number of the transferee and Holder will surrender this Warrant to the Company for reissuance to the transferee(s) (and Holder if applicable); and provided further, that any subsequent transferee other than SVB Financial Group shall agree in writing with the Company to be bound by all of the terms and conditions of this Warrant.

5.5 Notices. All notices and other communications hereunder from the Company to the Holder, or vice versa, shall be deemed delivered and effective (i) when given personally, (ii) on the third (3rd) Business Day after being mailed by first-class registered or certified mail, postage prepaid, (iii) upon actual receipt if given by facsimile or electronic mail and such receipt is confirmed in writing by the recipient, or (iv) on the first Business Day following delivery to a reliable overnight courier service, courier fee prepaid, in any case at such address as may have been furnished to the Company or Holder, as the case may be, in writing by the Company or such Holder from time to time in accordance with the provisions of this Section 5.5. All notices to Holder shall be addressed as follows until the Company receives notice of a change of address in connection with a transfer or otherwise:

SVB Financial Group
Attn: Treasury Department
3003 Tasman Drive, HC 215
Santa Clara, CA 95054
Telephone: (408) 654-7400
Facsimile: (408) 988-8317
Email address: derivatives@svb.com

Notice to the Company shall be addressed as follows until Holder receives notice of a change in address:

ATYR PHARMA, INC.
3545 John Hopkins Court, Suite 250
San Diego, CA 92121
Attn: John Mendlein, Ph.D, CEO
Fax: (858) 731-8394
Email: jemendlein@atyrpharma.com

With a copy (which shall not constitute notice) to:

Goodwin Proctor LLP
Three Embarcadero Center
San Francisco, CA 94111
Attn: Mitzi Chang
Fax: (415) 384-6006
Email: MChang@goodwinlaw.com

5.6 Waiver. This Warrant and any term hereof may be changed, waived, discharged or terminated (either generally or in a particular instance and either retroactively or prospectively) only by an instrument in writing signed by the party against which enforcement of such change, waiver, discharge or termination is sought.

5.7 Attorney's Fees. In the event of any dispute between the parties concerning the terms and provisions of this Warrant, the party prevailing in such dispute shall be entitled to collect from the other party all costs incurred in such dispute, including reasonable attorneys' fees.

5.8 Counterparts; Facsimile/Electronic Signatures. This Warrant may be executed in counterparts, all of which together shall constitute one and the same agreement. Any signature page delivered electronically or by facsimile shall be binding to the same extent as an original signature page with regards to any agreement subject to the terms hereof or any amendment thereto.

5.9 Governing Law. This Warrant shall be governed by and construed in accordance with the laws of the State of California, without giving effect to its principles regarding conflicts of law.

5.10 Headings. The headings in this Warrant are for purposes of reference only and shall not limit or otherwise affect the meaning of any provision of this Warrant.

5.11 Business Days. "**Business Day**" is any day that is not a Saturday, Sunday or a day on which Silicon Valley Bank is closed.

[Remainder of page left blank intentionally]
[Signature page follows]

IN WITNESS WHEREOF, the parties have caused this Warrant to Purchase Common Stock to be executed by their duly authorized representatives effective as of the Issue Date written above.

"COMPANY"

ATYR PHARMA, INC.

By: /s/ John Blake

Name: John Blake
(Print)
Title: VP Finance

"HOLDER"

SILICON VALLEY BANK

By: /s/ Anthony Flores

Name: Anthony Flores
(Print)
Title: Director

[Signature Page to Warrant]

APPENDIX 1

NOTICE OF EXERCISE

1. The undersigned Holder hereby exercises its right purchase _____ shares of the Common Stock of ATYR PHARMA, INC. (the "**Company**") in accordance with the attached Warrant To Purchase Common Stock, and tenders payment of the aggregate Warrant Price for such shares as follows:

[ ] check in the amount of $_____ payable to order of the Company enclosed herewith

[ ] Wire transfer of immediately available funds to the Company's account

[ ] Cashless Exercise pursuant to Section 1.2 of the Warrant

[ ] Other [Describe] _____

2. Please issue a certificate or certificates representing the Shares in the name specified below:

_____
Holder's Name

_____

_____
(Address)

3. By its execution below and for the benefit of the Company, Holder hereby restates each of the representations and warranties in Section 4 of the Warrant to Purchase Common Stock as of the date hereof.

HOLDER:

By:

Name:

Title:

(Date):

Exhibit 4.6

THIS WARRANT AND THE SHARES ISSUABLE HEREUNDER HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE "ACT"), OR THE SECURITIES LAWS OF ANY STATE AND, EXCEPT AS SET FORTH IN SECTION 5.3 BELOW, MAY NOT BE OFFERED, SOLD, PLEDGED OR OTHERWISE TRANSFERRED UNLESS AND UNTIL REGISTERED UNDER SAID ACT AND LAWS OR IN FORM AND SUBSTANCE SATISFACTORY TO THE COMPANY, SUCH OFFER, SALE, PLEDGE OR OTHER TRANSFER IS EXEMPT FROM SUCH REGISTRATION.

WARRANT TO PURCHASE COMMON STOCK

Company: ATYR PHARMA, INC.
Number of Shares of Common Stock: 47,771
Warrant Price: $3.14
Issue Date: November 18, 2016
Expiration Date: November 18, 2023 **See also Section 5.1(b).**
Credit Facility: This Warrant to Purchase Common Stock ("**Warrant**") is issued in connection with that certain Loan and Security Agreement of even date herewith between Solar Capital Ltd. and the Company (the "**Loan Agreement**").

THIS WARRANT CERTIFIES THAT, for good and valuable consideration, SOLAR CAPITAL LTD. (together with any successor or permitted assignee or transferee of this Warrant or of any shares issued upon exercise hereof, "**Holder**") is entitled to purchase the number of fully paid and non-assessable shares (the "**Shares**") of the above-stated common stock (the "**Common Stock**") of the above-named company (the "**Company**") at the above-stated Warrant Price, all as set forth above and as adjusted pursuant to Section 2 of this Warrant, subject to the provisions and upon the terms and conditions set forth in this Warrant.

SECTION 1. EXERCISE.

1.1 Method of Exercise. Holder may at any time and from time to time through 5:00 PM Pacific Time on the Expiration Date exercise this Warrant, in whole or in part, by delivering to the Company the original of this Warrant together with a duly executed Notice of Exercise in substantially the form attached hereto as Appendix 1 and, unless Holder is exercising this Warrant pursuant to a cashless exercise set forth in Section 1.2, a check, wire transfer of same-day funds (to an account designated by the Company), or other form of payment acceptable to the Company for the aggregate Warrant Price for the Shares being purchased.

1.2 Cashless Exercise. On any exercise of this Warrant, in lieu of payment of the aggregate Warrant Price in the manner as specified in Section 1.1 above, but otherwise in accordance with the requirements of Section 1.1, Holder may elect to receive Shares equal to the value of this Warrant, or portion hereof as to which this Warrant is being exercised as set forth in the following sentence. Thereupon, the Company shall issue to the Holder such number of fully paid and non-assessable Shares as are computed using the following formula:

$$X = Y(A-B)/A$$

where:

X = the number of Shares to be issued to the Holder;

Y = the number of Shares with respect to which this Warrant is being exercised (inclusive of the Shares surrendered to the Company in payment of the aggregate Warrant Price);

A = the Fair Market Value (as determined pursuant to Section 1.3 below) of one Share; and

B = the Warrant Price.

1.3 Fair Market Value. If the Company's Common Stock is then traded or quoted on a nationally recognized securities exchange, inter-dealer quotation system or over-the-counter market (a "**Trading Market**"), the fair market value of a Share shall be the closing price or last sale price of a share of Common Stock reported for the Business Day immediately before the date on which Holder delivers this Warrant together with its Notice of Exercise to the Company. If the Company's Common Stock is not traded in a Trading Market, the Board of Directors of the Company shall determine the fair market value of a Share in its reasonable good faith judgment.

1.4 Delivery of Certificate and New Warrant. Within a reasonable time after Holder exercises this Warrant in the manner set forth in Section 1.1 or 1.2 above, the Company shall deliver to Holder a certificate representing the Shares issued to Holder upon such exercise and, if this Warrant has not been fully exercised and has not expired, a new warrant of like tenor representing the Shares not so acquired.

1.5 Replacement of Warrant. On receipt of evidence reasonably satisfactory to the Company of the loss, theft, destruction or mutilation of this Warrant and, in the case of loss, theft or destruction, on delivery of an indemnity agreement reasonably satisfactory in form, substance and amount to the Company or, in the case of mutilation, on surrender of this Warrant to the Company for cancellation, the Company shall, within a reasonable time, execute and deliver to Holder, in lieu of this Warrant, a new warrant of like tenor and amount.

1.6 Treatment of Warrant Upon Acquisition of Company.

(a) Acquisition. For the purpose of this Warrant, "**Acquisition**" means any transaction or series of related transactions involving: (i) the sale, lease, exclusive license, or other disposition of all or substantially all of the assets of the Company (ii) any merger or consolidation of the Company into or with another person or entity (other than a merger or consolidation effected exclusively to change the Company's domicile), or any other corporate reorganization, in which the stockholders of the Company in their capacity as such immediately prior to such merger, consolidation or reorganization, own less than a majority of the Company's (or the surviving or successor entity's) outstanding voting power immediately after such merger, consolidation or reorganization; or (iii) any sale or other transfer by the stockholders of the Company of shares representing at least a majority of the Company's then-total outstanding combined voting power.

(b) Treatment of Warrant at Acquisition. In the event of an Acquisition in which the consideration to be received by the Company's stockholders consists solely of cash, solely of Marketable Securities or a combination of cash and Marketable Securities (a "**Cash/Public Acquisition**"), and the fair market value of one Share as determined in accordance with Section 1.3 above would be greater than the Warrant Price in effect on such date immediately prior to such Cash/Public Acquisition, and Holder has not exercised this Warrant pursuant to Section 1.1 above as to all Shares, then this Warrant shall automatically be deemed to be Cashless Exercised pursuant to Section 1.2 above as to all Shares effective immediately prior to and contingent upon the consummation of a Cash/Public Acquisition. In connection with such Cashless Exercise, Holder shall be deemed to have restated each of the representations and warranties in Section 4 of the Warrant as the date thereof and the Company shall promptly notify the Holder of the number of Shares (or such other securities) issued upon exercise. In the event of a Cash/Public Acquisition where the fair market value of one Share as determined in accordance with Section 1.3 above would be less than the Warrant Price in effect immediately prior to such Cash/Public Acquisition, then this Warrant will expire immediately prior to the consummation of such Cash/Public Acquisition.

(c) Upon the closing of any Acquisition other than a Cash/Public Acquisition defined above, the acquiring, surviving or successor entity shall assume the obligations of this Warrant, and this Warrant shall thereafter be exercisable for the same securities and/or other property as would have been paid for the Shares issuable upon exercise of the unexercised portion of this Warrant as if such Shares were outstanding on and as of the closing of such Acquisition, subject to further adjustment from time to time in accordance with the provisions of this Warrant.

(d) As used in this Warrant, "**Marketable Securities**" means securities meeting all of the following requirements: (i) the issuer thereof is then subject to the reporting requirements of Section 13 or Section 15(d) of the Securities Exchange Act of 1934, as amended (the "**Exchange Act**"), and is then current in its filing of all required reports and other information under the Act and the Exchange Act; (ii) the class and series of shares or other security of the issuer that would be received by Holder in connection with the Acquisition were Holder to exercise this Warrant on or prior to the closing thereof is then traded in a Trading Market, and (iii) following the closing of such Acquisition, Holder would not be restricted from publicly re-selling all of the issuer's shares and/or other securities that would be received by Holder in such Acquisition were Holder to exercise or convert this Warrant in full on or prior to the closing of such Acquisition, except to the extent that any such restriction (x) arises solely under federal or state securities laws, rules or regulations, and (y) does not extend beyond six (6) months from the closing of such Acquisition.

SECTION 2. ADJUSTMENTS TO THE SHARES AND WARRANT PRICE.

2.1 Stock Dividends, Splits, Etc. If the Company declares or pays a dividend or distribution on the outstanding shares of the Common Stock payable in securities or property (other than cash), then upon exercise of this Warrant, for each Share acquired, Holder shall receive, without additional cost to Holder, the total number and kind of securities and property which Holder would have received had Holder owned the Shares of record as of the date the dividend or distribution occurred. If the Company subdivides the outstanding shares of the Common Stock by reclassification or otherwise into a greater number of shares, the number of Shares purchasable hereunder shall be proportionately increased and the Warrant Price shall be proportionately decreased. If the outstanding shares of the Common Stock are combined or consolidated, by reclassification or otherwise, into a lesser number of shares, the Warrant Price shall be proportionately increased and the number of Shares shall be proportionately decreased.

2.2 Reclassification, Exchange, Combinations or Substitution. Upon any event whereby all of the outstanding shares of the Common Stock are reclassified, exchanged, combined, substituted, or replaced for, into, with or by Company securities of a different class and/or series, then from and after the consummation of such event, this Warrant will be exercisable for the number, class and series of Company securities that Holder would have received had the Shares been outstanding on and as of the consummation of such event, and subject to further adjustment thereafter from time to time in accordance with the provisions of this Warrant. The provisions of this Section 2.2 shall similarly apply to successive reclassifications, exchanges, combinations substitutions, replacements or other similar events.

2.3 Intentionally Omitted.

2.4 Intentionally Omitted.

2.5 No Fractional Share. No fractional Share shall be issuable upon exercise of this Warrant and the number of Shares to be issued shall be rounded down to the nearest whole Share. If a fractional Share interest arises upon any exercise of the Warrant, the Company shall eliminate such fractional Share interest by paying Holder in cash the amount computed by multiplying the fractional interest by (i) the fair market value (as determined in accordance with Section 1.3 above) of a full Share, less (ii) the then-effective Warrant Price.

2.6 Notice/Certificate as to Adjustments. Upon each adjustment of the Warrant Price, Common Stock and/or number of Shares, the Company, at the Company's expense, shall notify Holder in writing within a reasonable time setting forth the adjustments to the Warrant Price, class and/or number of Shares and facts upon which such adjustment is based. The Company shall, upon written request from Holder, furnish Holder with a certificate of its Chief Financial Officer, including computations of such adjustment and the Warrant Price, class and number of Shares in effect upon the date of such adjustment.

SECTION 3. REPRESENTATIONS AND COVENANTS OF THE COMPANY.

3.1 Representations and Warranties. The Company represents and warrants to, and agrees with, the Holder as follows:

(a) The initial Warrant Price referenced on the first page of this Warrant is not greater than the price per share at which shares of Company Common Stock or options to purchase shares of Company Common Stock were issued immediately prior to the Issue Date hereof.

(b) All Shares which may be issued upon the exercise of this Warrant, shall, upon issuance, be duly authorized, validly issued, fully paid and non-assessable, and free of any liens and encumbrances except for restrictions on transfer provided for herein or under applicable federal and state securities laws. The Company covenants that it shall at all times cause to be reserved and kept available out of its authorized and unissued capital stock such number of securities as will be sufficient to permit the exercise in full of this Warrant.

3.2 Notice of Certain Events. If the Company proposes at any time to:

(a) declare any dividend or distribution upon the outstanding shares of the Company's stock, whether in cash, property, stock, or other securities and whether or not a regular cash dividend;

(b) offer for subscription or sale pro rata to the holders of the outstanding shares any additional shares of any class or series of the Company's stock (other than pursuant to contractual pre-emptive rights);

(c) effect any reclassification, exchange, combination, substitution, reorganization or recapitalization of the outstanding shares of the Common Stock; or

(d) effect an Acquisition or to liquidate, dissolve or wind up;

then, in connection with each such event, the Company shall give Holder:

(1) in the case of the matters referred to in (a) and (b) above, at least seven (7) Business Days prior written notice of the earlier to occur of the effective date thereof or the date on which a record will be taken for such dividend, distribution, or subscription rights (and specifying the date on which the holders of outstanding shares of the Common Stock will be entitled thereto) or for determining rights to vote, if any, and

(2) in the case of the matters referred to in (c) and (d) above at least seven (7) Business Days prior written notice of the date when the same will take place (and specifying the date on which the holders of outstanding shares of the Class will be entitled to exchange their shares for the securities or other property deliverable upon the occurrence of such event and such reasonable information as Holder may reasonably require regarding the treatment of this Warrant in connection with such event giving rise to the notice).

Company will also provide information requested by Holder that is reasonably necessary to enable Holder to comply with Holder's accounting or reporting requirements.

SECTION 4. REPRESENTATIONS, WARRANTIES OF THE HOLDER.

The Holder represents and warrants to the Company as follows:

4.1 Purchase for Own Account. This Warrant and the Shares to be acquired upon exercise of this Warrant by Holder are being acquired for investment for Holder's account, not as a nominee or agent, and not with a view to the public resale or distribution within the meaning of the Act. Holder also represents that it has not been formed for the specific purpose of acquiring this Warrant or the Shares.

4.2 Disclosure of Information. Holder is aware of the Company's business affairs and financial condition and has received or has had full access to all the information it considers necessary or appropriate to make an informed investment decision with respect to the acquisition of this Warrant and its underlying securities. Holder further has had an opportunity to ask questions and receive answers from the Company regarding the terms and conditions of the offering of this Warrant and its underlying securities and to obtain additional information (to the extent the Company possessed such information or could acquire it without unreasonable effort or expense) necessary to verify any information furnished to Holder or to which Holder has access.

4.3 Investment Experience. Holder understands that the purchase of this Warrant and its underlying securities involves substantial risk. Holder has experience as an investor in securities of companies in the development stage and acknowledges that Holder can bear the economic risk of such Holder's investment in this Warrant and its underlying securities and has such knowledge and experience in financial or business matters that Holder is capable of evaluating the merits and risks of its investment in this Warrant and its underlying securities and/or has a preexisting personal or business relationship with the Company and certain of its officers, directors or controlling persons of a nature and duration that enables Holder to be aware of the character, business acumen and financial circumstances of such persons.

4.4 Accredited Investor Status. Holder is an "accredited investor" within the meaning of Regulation D promulgated under the Act.

4.5 The Act. Holder understands that this Warrant and the Shares issuable upon exercise hereof have not been registered under the Act in reliance upon a specific exemption therefrom, which exemption depends upon, among other things, the bona fide nature of the Holder's investment intent as expressed herein. Holder understands that this Warrant and the Shares issued upon any exercise hereof must be held indefinitely unless subsequently registered under the Act and qualified under applicable state securities laws, or unless exemption from such registration and qualification are otherwise available. Holder is aware of the provisions of Rule 144 promulgated under the Act.

4.6 No Voting Rights. Holder, as a Holder of this Warrant, will not have any voting rights or other rights as a stockholder until the exercise of this Warrant.

SECTION 5. MISCELLANEOUS.

5.1 Term and Automatic Conversion Upon Expiration.

(a) Term. Subject to the provisions of Section 1.6 above, this Warrant is exercisable in whole or in part at any time and from time to time on or before 6:00 PM, Pacific time, on the Expiration Date and shall be void thereafter.

(b) Automatic Cashless Exercise upon Expiration. In the event that, upon the Expiration Date, the fair market value of one Share (or other security issuable upon the exercise hereof) as determined in accordance with Section 1.3 above is greater than the Warrant Price in effect on such date, then this Warrant shall automatically be deemed on and as of such date to be exercised pursuant to Section 1.2 above as to all Shares (or such other securities) for which it shall not previously have been exercised, and the Company shall, within a reasonable time, cause its transfer agent and registrar to register in book-entry format or to deliver to Holder a certificate representing the Shares (or such other securities) issued upon such exercise to Holder.

5.2 Legends. The Shares shall be imprinted with a legend in substantially the following form:

> THE SHARES EVIDENCED BY THIS CERTIFICATE HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE "**ACT**"), OR THE SECURITIES LAWS OF ANY STATE AND, EXCEPT AS SET FORTH IN THAT CERTAIN WARRANT TO PURCHASE COMMON STOCK ISSUED BY THE ISSUER TO SOLAR CAPITAL LTD. DATED NOVEMBER 18, 2016, MAY NOT BE OFFERED, SOLD, PLEDGED OR OTHERWISE TRANSFERRED UNLESS AND UNTIL REGISTERED UNDER SAID ACT AND LAWS OR IN FORM AND SUBSTANCE SATISFACTORY TO THE ISSUER, SUCH OFFER, SALE, PLEDGE OR OTHER TRANSFER IS EXEMPT FROM SUCH REGISTRATION.

5.3 Compliance with Securities Laws on Transfer. This Warrant and the Shares issuable upon exercise of this Warrant may not be transferred or assigned in whole or in part except in compliance with applicable federal and state securities laws by the transferor and the transferee (including, without limitation, the delivery of investment representation letters and legal opinions reasonably satisfactory to the Company, as reasonably requested by the Company).

5.4 Intentionally Omitted.

5.5 Notices. All notices and other communications hereunder from the Company to the Holder, or vice versa, shall be deemed delivered and effective (i) when given personally, (ii) on the third (3rd) Business Day after being mailed by first-class registered or certified mail, postage prepaid, (iii) upon actual receipt if given by facsimile or electronic mail and such receipt is confirmed in writing by the recipient, or (iv) on the first Business Day following delivery to a reliable overnight courier service, courier fee prepaid, in any case at such address as may have been furnished to the Company or Holder, as the case may be, in writing by the Company or such Holder from time to time in accordance with the provisions of this Section 5.5. All notices to Holder shall be addressed as follows until the Company receives notice of a change of address in connection with a transfer or otherwise:

SOLAR CAPITAL LTD.
500 Park Avenue, 3rd Floor
New York, New York 10022
Attn: Neil Bonanno, Managing Director
Fax: (212) 993-1698
Email: bonanno@solarcapltd.com

Notice to the Company shall be addressed as follows until Holder receives notice of a change in address:

ATYR PHARMA, INC.
3545 John Hopkins Court, Suite 250
San Diego, CA 92121
Attn: John Mendlein, Ph.D, CEO
Fax: (858) 731-8394
Email: jemendlein@atyrpharma.com

With a copy (which shall not constitute notice) to:

Goodwin Proctor LLP
Three Embarcadero Center
San Francisco, CA 94111
Attn: Mitzi Chang
Fax: (415) 384-6006
Email: MChang@goodwinlaw.com

5.6 Waiver. This Warrant and any term hereof may be changed, waived, discharged or terminated (either generally or in a particular instance and either retroactively or prospectively) only by an instrument in writing signed by the party against which enforcement of such change, waiver, discharge or termination is sought.

5.7 Attorney's Fees. In the event of any dispute between the parties concerning the terms and provisions of this Warrant, the party prevailing in such dispute shall be entitled to collect from the other party all costs incurred in such dispute, including reasonable attorneys' fees.

5.8 Counterparts; Facsimile/Electronic Signatures. This Warrant may be executed in counterparts, all of which together shall constitute one and the same agreement. Any signature page delivered electronically or by facsimile shall be binding to the same extent as an original signature page with regards to any agreement subject to the terms hereof or any amendment thereto.

5.9 Governing Law. This Warrant shall be governed by and construed in accordance with the laws of the State of California, without giving effect to its principles regarding conflicts of law.

5.10 Headings. The headings in this Warrant are for purposes of reference only and shall not limit or otherwise affect the meaning of any provision of this Warrant.

5.11 Business Days. "**Business Day**" is any day that is not a Saturday, Sunday or a day on which Silicon Valley Bank is closed.

[Remainder of page left blank intentionally]
[Signature page follows]

IN WITNESS WHEREOF, the parties have caused this Warrant to Purchase Common Stock to be executed by their duly authorized representatives effective as of the Issue Date written above.

"COMPANY"

ATYR PHARMA, INC.

By: /s/ John Blake

Name: John Blake
(Print)
Title: VP Finance

"HOLDER"

SOLAR CAPITAL LTD.

By: /s/ Anthony J. Storino

Name: Anthony J. Storino
(Print)
Title: Authorized Signatory

[Signature Page to Warrant]

APPENDIX 1

NOTICE OF EXERCISE

1. The undersigned Holder hereby exercises its right purchase _____ shares of the Common Stock of ATYR PHARMA, INC. (the "**Company**") in accordance with the attached Warrant To Purchase Common Stock, and tenders payment of the aggregate Warrant Price for such shares as follows:

[ ] check in the amount of $_____ payable to order of the Company enclosed herewith

[ ] Wire transfer of immediately available funds to the Company's account

[ ] Cashless Exercise pursuant to Section 1.2 of the Warrant

[ ] Other [Describe] _____

2. Please issue a certificate or certificates representing the Shares in the name specified below:

_____
Holder's Name

_____

_____
(Address)

3. By its execution below and for the benefit of the Company, Holder hereby restates each of the representations and warranties in Section 4 of the Warrant to Purchase Common Stock as of the date hereof.

HOLDER:

By:

Name:

Title:

(Date):

Exhibit 10.8

FIRST AMENDMENT TO LEASE

THIS FIRST AMENDMENT TO LEASE (this "Amendment") is entered into as of this 4th day of January, 2017, by and between BMR-3545-3575 JOHN HOPKINS LP, a Delaware limited partnership ("Landlord," as successor-in-interest to BMR-John Hopkins Court LLC), and ATYR PHARMA, INC., a Delaware corporation ("Tenant").

RECITALS

A. WHEREAS, Landlord and Tenant are parties to that certain Lease dated as of December 22, 2011 (as the same may have been amended, supplemented or modified from time to time, the "Existing Lease"), whereby Tenant leases certain premises (the "Premises") from Landlord at 3545-3575 John Hopkins Court in San Diego, California (the "Building");

B. WHEREAS, Landlord and Tenant desire to extend the Term;

C. WHEREAS, Landlord desires to grant Tenant an option to expand into additional premises at the Building; and

D. WHEREAS, Landlord and Tenant desire to modify and amend the Existing Lease only in the respects and on the conditions hereinafter stated.

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. Definitions. For purposes of this Amendment, capitalized terms shall have the meanings ascribed to them in the Existing Lease unless otherwise defined herein. The Existing Lease, as amended by this Amendment, is referred to collectively herein as the "Lease." From and after the date hereof, the term "Lease," as used in the Existing Lease, shall mean the Existing Lease, as amended by this Amendment.

2. Extension Term. The Term is hereby extended by twenty-four (24) months and the Term Expiration Date is hereby amended to be May 15, 2019. The period of time from May 16, 2017 through the new Term Expiration Date is referred to herein as the "Extension Term."

3. Base Rent. Tenant shall pay Base Rent to Landlord during the Extension Term in accordance with the provisions of the Lease. Commencing as of the first day of the Extension Term, Base Rent for the Premises shall be as set forth in the chart below:

Dates	Square Feet of Rentable Area	Base Rent per Square Foot of Rentable Area	Monthly Base Rent	Annual Base Rent
May 16, 2017 – May 15, 2018	17,083	$3.70 monthly	$63,207.10	$758,485.20
May 16, 2018 – May 15, 2019	17,083	$3.81 monthly	$65,086.23	$781,034.76

4. Additional Rent. During the Extension Term, in addition to Base Rent, Tenant shall continue to pay to Landlord as Additional Rent at times specified in the Lease (a) Tenant's Share of Operating Expenses, (b) the Property Management Fee and (c) any other amounts that Tenant assumes or agrees to pay under the provisions of the 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 the Lease to be performed by Tenant, after notice and the lapse of any applicable cure periods.

5. Condition of Premises. Tenant acknowledges that (a) it is in possession of and is fully familiar with the condition of the Premises and, notwithstanding anything contained in the Lease to the contrary, agrees to take the same in its condition "as is" as of the first day of the Extension Term, and (b) Landlord shall have no obligation to alter, repair or otherwise prepare the Premises for Tenant's continued occupancy for the Extension Term or to pay for any improvements to the Premises, except as may be expressly provided in the Lease.

6. Expansion Option.

6.1. Subject to the conditions set forth in this Article, and subject to any other parties' pre-existing rights with respect to the Expansion Space (as defined below), Tenant shall have the right, but not the obligation, to expand the Premises (the "Expansion Option") to include approximately seven thousand four hundred eleven (7,411) square feet of Rentable Area on the first (1st) floor of the Building as more particularly shown on the floor plan attached hereto as Exhibit A (the "Expansion Space").

6.2. Tenant may exercise the Expansion Option by providing Landlord, no later than March 31, 2017 (the "Expansion Notice Deadline"), with written notice that Tenant has elected to exercise the Expansion Option. Within ten (10) days after exercising the Expansion Option, Tenant and Landlord shall enter into a written amendment to the Lease (the "Expansion Amendment"), which amendment shall provide, unless otherwise agreed in writing, (a) that, subject to Section 6.5 below, the commencement date of the Expansion Space shall be the later of (i) July 1, 2017 and (ii) the day after the date that Regulus (as defined below) surrenders the Expansion Space to Landlord in accordance with the terms of Regulus' lease with Landlord, (b) that the Premises shall be increased to include the square feet of Rentable Area of the Expansion Space, (c) the new Base Rent, which Expansion Space Base Rent shall be at the then-current base rental rate per square foot of Rentable Area for the Premises under the Lease (and shall be escalated at the same rate and at the same time as the base rental rate escalations for the Premises), (d) Tenant's new Pro Rata Share of Operating Expenses based upon the addition of the Expansion Space to the Premises, and (e) the proportionate increase to the Security Deposit such that the Security Deposit is an amount equal to one (1) month of Base Rent for the entire Premises (i.e., the Premises plus the Expansion Space) (which increase shall be payable to Landlord upon execution of the Expansion Amendment). In all other respects, this Lease shall remain in full force and effect, and shall (except with regard to (y) any obligation of Landlord in connection with the Tenant Improvements and the TI Allowance and (z) the first (1st) sentence of Article 5 of the Lease) apply to the Expansion Space. Time shall be of the essence as to Tenant's exercise of the Expansion Option. Tenant assumes full responsibility for maintaining a record of the deadlines to exercise the Expansion Option. Tenant acknowledges that it would be inequitable to require Landlord to accept any exercise of the Expansion Option after the Expansion Notice Deadline.

6.3. Notwithstanding anything in this Article to the contrary, Tenant shall not exercise the Expansion Option during such period of time that Tenant is in default under any provision of the Lease. Any attempted exercise of the Expansion Option during a period of time in which Tenant is so in default shall be void and of no effect. In addition, Tenant shall not be entitled to exercise the Expansion Option if Landlord has given Tenant two (2) or more notices of default under the Lease, whether or not the defaults are cured, during the twelve (12) month period prior to the date on which Tenant seeks to exercise the Expansion Option.

6.4. Notwithstanding anything in this Lease to the contrary, the Expansion Option shall expire on March 31, 2017.

6.5. Tenant acknowledges that the Expansion Space is currently leased to Regulus Therapeutics Inc. ("Regulus") and that Regulus' lease with Landlord for the Expansion Space is currently scheduled to expire on June 30, 2017. Tenant agrees that any Expansion Amendment will provide that in the event of Regulus' failure to surrender the Expansion Space in accordance with the terms of its lease with Landlord for any reason, then (a) such Expansion Amendment shall not be void or voidable, (b) Landlord shall not be liable to Tenant for any loss or damage resulting therefrom, and (c) Tenant shall not be responsible for the payment of any Base Rent or Tenant's Share of Operating Expenses (as defined below), in each case with respect to the Expansion Space only, until the actual commencement date of the Expansion Space occurs.

7. New Lease. If Tenant requires additional space for its operations, and either (a) Landlord cannot accommodate such additional space within the Project or (b) Landlord can accommodate such additional space within the Project, but Landlord and Tenant are unable to mutually agree upon acceptable terms for such additional space within the Project, and if Landlord (or an affiliate of Landlord) and Tenant are able to negotiate mutually acceptable terms for the lease of additional space (which shall not be less than thirty thousand (30,000) square feet of Rentable Area for a term of not less than five (5) years; and provided that the rental rate for such additional space shall equal FMV (provided that if such space is not in the Torrey Pines submarket, then the applicable submarket shall be used in connection with the determination of FMV) for such space) at a property owned by Landlord (or an affiliate of Landlord) (the "New Lease"), then upon the full execution of such New Lease, Tenant shall have the unilateral right to terminate the Lease without penalty or termination fee. Such right shall be exercised by Tenant's delivery to Landlord of written notice of termination not later than thirty (30) days after full execution and delivery of the New Lease and such notice shall specify the effective date of such termination. Neither party shall have any obligation to enter into or negotiate for the New Lease.

8. Notice of Third Party Agreement. In the event Tenant (or any affiliate of Tenant) intends to enter into any lease agreement (including a letter of intent) with any entity not affiliated with Landlord (an "Unaffiliated Entity") for space in the San Diego area in excess of one thousand (1,000) square feet, then at least thirty (30) days prior to Tenant's (or Tenant's affiliate's, as applicable) execution of any such agreement, Tenant shall provide written notice thereof to Landlord. In addition, neither Tenant nor any affiliate of Tenant shall enter into any such lease agreement (including a letter of intent) with an Unaffiliated Entity unless Tenant has provided such prior notice to Landlord and Landlord has had the opportunity, if Landlord so elects (but without any obligation to do so), to present to Tenant (or Tenant's affiliate, as applicable) a proposal to lease alternative premises which satisfies in part or in its entirety the premises being sought by Tenant or Tenant's affiliate (" Alternative Premises") on market terms at the Project or, if Landlord so elects (but without any obligation to do so), at another property in the San Diego area owned or controlled by an affiliate of Landlord. Tenant (on behalf of itself and any such affiliate) agrees to consider any Alternative Premises proposed by Landlord or an affiliate of Landlord; provided, however, that the final decision regarding the leasing of any such additional space from Landlord, any affiliate of Landlord or an Unaffiliated Entity shall be made by Tenant (or Tenant's affiliate, as applicable) in its good faith, but sole discretion. For purposes of clarity, Landlord shall have no obligation to propose terms for, enter into or negotiate for a lease of Alternative Premises.

9. Hazardous Materials. The first instance of Section 21.1(a) of the Lease is hereby modified by inserting the word "not" after "Premises" and before "caused."

10. Alterations. Pursuant to that certain letter dated December 20, 2016, a copy of which is attached hereto as Exhibit B (the "Alterations Approval Letter"), Landlord requires that, prior to the expiration or earlier termination of the Lease, certain alterations and improvements (the "2016 Alterations") will need to be removed and the Premises restored. However, in the event that the Term of the Lease is extended to or beyond May 15, 2022 by a fully executed written amendment to the Lease, then notwithstanding such removal provision in the Alterations Approval Letter, Tenant shall not be required to remove the 2016 Alterations upon the expiration or earlier termination of the Lease; provided, however, that neither Landlord nor Tenant has any obligation to agree to or negotiate for any such extension.

11. Broker. Tenant represents and warrants that it has not dealt with any broker or agent in the negotiation for or the obtaining of this Amendment, other than Hughes Marino ("Tenant Broker") and Jones Lang LaSalle ("Landlord Broker," and together with Tenant Broker, "Brokers"), and agrees to reimburse, indemnify, save, defend (at Landlord's option and with counsel reasonably acceptable to Landlord, at Tenant's sole cost and expense) and hold harmless the Landlord Indemnitees for, from and against any and all cost or liability for compensation claimed by any such broker or agent, other than Brokers, employed or engaged by Tenant or claiming to have been employed or engaged by Tenant. Brokers are entitled to a leasing commission in connection with the making of this Amendment, and Landlord shall pay (a) Tenant Broker's portion of such commission to Tenant Broker pursuant to a separate agreement between Landlord and Tenant Broker and (b) Landlord Broker's portion of such commission to Landlord Broker pursuant to a separate agreement between Landlord and Landlord Broker.

12. No Default. Tenant represents, warrants and covenants that, to the best of Tenant's knowledge, Landlord and Tenant are not in default of any of their respective obligations under the Existing Lease and no event has occurred that, with the passage of time or the giving of notice (or both) would constitute a default by either Landlord or Tenant thereunder.

13. Notices. Tenant confirms that, notwithstanding anything in the Lease to the contrary, notices delivered to Tenant pursuant to the Lease should be sent to:

aTyr Pharma, Inc.
3545 John Hopkins Court
San Diego, California 92121
Attn: Vice President, Finance.

14. Effect of Amendment. Except as modified by this Amendment, the Existing Lease and all the covenants, agreements, terms, provisions and conditions thereof shall remain in full force and effect and are hereby ratified and affirmed. In the event of any conflict between the terms contained in this Amendment and the Existing Lease, the terms herein contained shall supersede and control the obligations and liabilities of the parties.

15. Successors and Assigns. Each of the covenants, conditions and agreements contained in this Amendment 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 and sublessees. Nothing in this section shall in any way alter the provisions of the Lease restricting assignment or subletting.

16. Miscellaneous. This Amendment becomes effective only upon execution and delivery hereof by Landlord and Tenant. The captions of the paragraphs and subparagraphs in this Amendment are inserted and included solely for convenience and shall not be considered or given any effect in construing the provisions hereof. All exhibits hereto are incorporated herein by reference. 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, lease amendment or otherwise until execution by and delivery to both Landlord and Tenant.

17. Authority. Tenant guarantees, warrants and represents that the individual or individuals signing this Amendment on behalf of Tenant have the power, authority and legal capacity to sign this Amendment 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. Landlord guarantees, warrants and represents that the individual or individuals signing this Amendment on behalf of Landlord have the power, authority and legal capacity to sign this Amendment 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.

18. Counterparts; Facsimile and PDF Signatures. This Amendment may be executed in one or more counterparts, each of which, when taken together, shall constitute one and the same document. A facsimile or portable document format (PDF) signature on this Amendment shall be equivalent to, and have the same force and effect as, an original signature.

[REMAINDER OF THIS PAGE INTENTIONALLY LEFT BLANK]

IN WITNESS WHEREOF, Landlord and Tenant have executed this Amendment as of the date and year first above written.

LANDLORD:

BMR-3545-3575 JOHN HOPKINS LP,
a Delaware limited partnership

By: /s/ Marie Lewis
Name: Marie Lewis
Title: Vice President, Legal

TENANT:

ATYR PHARMA, INC.,
a Delaware corporation

By: /s/ Nancy Denyes Krueger
Name: Nancy Denyes Krueger
Title: Vice President, Legal Affairs

EXHIBIT A

EXPANSION SPACE

[See attached]

EXHIBIT B

ALTERATIONS APPROVAL LETTER

[See attached]

BMR-3545-3575 John Hopkins LP

17190 Bernardo Center Drive • San Diego, California 92 128
Phone: (858) 485-9840 • Facsimile: (858)485-98•13

VIA FEDERAL EXPRESS

December 20, 2016

aTyr Pharma, Inc.
3545 John Hopkins Court, Suite 250
San Diego, Ca 92121
Attn: Vice President, Operations

Re; Approval of Alterations at 3545 John Hopkins Court, San Diego, CA 92121

To Whom It May Concern:

aTyr Pharma, Inc. a Delaware corporation ("aTyr Pharma, Inc.") has requested approval of the following: (a) Back's Construction Inc., Proposal Number 2299, dated December 7, 2016 and (b) Floor Plan of Suite 250 indicating the removal of two (2) partition walls, relocating a door and extending the vacuum lines from the existing west lab into the two newly enlarged rooms within the vivarium (the "Documents").

Pursuant to Section 17 of the Lease dated December 22, 2011 (the "Lease"), between BMR-3545-3575 John Hopkins LP a Delaware limited partnership ("BMR"), and aTyr Pharma, Inc., this letter constitutes Landlord's written approval of the Documents.

aTyr Pharma, Inc., hereby confirms that, prior to the expiration or earlier termination of the Lease, the new alterations or improvements would need to be removed and the premises restored.

Review or approval of the Documents by BMR shall not relieve aTyr Pharma, Inc. of its responsibilities under the Lease, or be deemed to be an approval by BMR of any deviation from, or waiver by BMR of aTyr Pharma, Inc's failure to comply with (a) any provision or requirement of the Lease, unless such deviation or failure has been conspicuously, specifically and clearly identified as such (with a reasonably descriptive explanation of the nature of such deviation or failure) in writing in the Documents or (b) applicable laws or permits.

If you have any questions, please do not hesitate to contact Shelby Dolan at 858.207.5943.

Sincerely,

/s/ Marie Lewis
Marie Lewis
Vice President, Legal

cc: Kevin Tremblay
John Bonnano
Shelby Dolan

Exhibit 10.17

CERTAIN CONFIDENTIAL PORTIONS OF THIS EXHIBIT WERE OMITTED AND REPLACED WITH "[***]". A COMPLETE VERSION OF THIS EXHIBIT HAS BEEN FILED SEPARATELY WITH THE SECRETARY OF THE SECURITIES AND EXCHANGE COMMISSION PURSUANT TO AN APPLICATION REQUESTING CONFIDENTIAL TREATMENT UNDER RULE 24B-2 OF THE EXCHANGE ACT OF 1934

LOAN AND SECURITY AGREEMENT

THIS LOAN AND SECURITY AGREEMENT (as the same may from time to time be amended, modified, supplemented or restated, this "**Agreement**") dated as of November 18, 2016 (the "**Effective Date**") among SILICON VALLEY BANK, a California corporation with an office located at 3003 Tasman Drive, Santa Clara, CA 95054 ("**Bank**" or "**SVB**"), as collateral agent (in such capacity, "**Collateral Agent**"), the Lenders listed on Schedule 1.1 hereof or otherwise a party hereto from time to time including Bank in its capacity as a Lender and SOLAR CAPITAL LTD., a Maryland corporation with an office located at 500 Park Avenue, 3rd Floor, New York, New York 10022 (" **Solar**" and, together with Bank, each a "**Lender**" and collectively, the "**Lenders**"), and ATYR PHARMA, INC., a Delaware corporation with an office located at 3545 John Hopkins Court, Suite 250, San Diego, CA 92121 ("**Borrower**"), provides the terms on which the Lenders shall lend to Borrower and Borrower shall repay the Lenders. The parties agree as follows:

1. ACCOUNTING AND OTHER TERMS

1.1 Accounting terms not defined in this Agreement shall be construed in accordance with GAAP. Calculations and determinations must be made in accordance with GAAP. Capitalized terms not otherwise defined in this Agreement shall have the meanings set forth in Section 13. All other terms contained in this Agreement, unless otherwise indicated, shall have the meaning provided by the Code to the extent such terms are defined therein. All references to "**Dollars**" or "**$**" are United States Dollars, unless otherwise noted.

2. LOANS AND TERMS OF PAYMENT

2.1 **Promise to Pay.** Borrower hereby unconditionally promises to pay each Lender, the outstanding principal amount of all Term Loans advanced to Borrower by such Lender and accrued and unpaid interest thereon and any other amounts due hereunder as and when due in accordance with this Agreement.

2.2 **Term Loans**.

(a) Availability.

(i) Subject to the terms and conditions of this Agreement, the Lenders agree, severally and not jointly, to make term loans to Borrower on the Effective Date in an aggregate original principal amount of Ten Million Dollars ($10,000,000.00) according to each Lender's Term A Loan Commitment as set forth on Schedule 1.1 hereto (such term loans are hereinafter referred to singly as a "**Term A Loan**", and collectively as the "**Term A Loans**"). After repayment, no Term A Loan may be re-borrowed.

(ii) Subject to the terms and conditions of this Agreement, the Lenders agree, severally and not jointly, during the Second Draw Period, to make term loans to Borrower in an aggregate original principal amount up to Five Million Dollars ($5,000,000.00) according to each Lender's Term B Loan Commitment as set forth on Schedule 1.1 hereto (such term loans are hereinafter referred to singly as a "**Term B Loan**", and collectively as the "**Term B Loans**"). After repayment, no Term B Loan may be re-borrowed.

(iii) Subject to the terms and conditions of this Agreement, the Lenders agree, severally and not jointly, during the Third Draw Period, to make term loans to Borrower in an aggregate original principal amount up to Five Million Dollars ($5,000,000.00) according to each Lender's Term C Loan Commitment as set forth on Schedule 1.1 hereto (such term loans are hereinafter referred to singly as a "**Term C Loan**", and collectively as the "**Term C Loans**"; each Term A Loan, Term B Loan or Term C Loan is hereinafter referred to singly as a " **Term Loan**" and the Term A Loans, the Term B Loans and the Term C Loans are hereinafter referred to collectively as the "**Term Loans**"). After repayment, no Term C Loan may be re-borrowed.

* Confidential information, indicated [***], has been omitted from this filing and filed separately with the Securities and Exchange Commission.

(b) Repayment. Borrower shall make monthly payments of interest only in arrears commencing on the first (1st) Payment Date following the Funding Date of each Term Loan, and continuing on the Payment Date of each successive month thereafter through and including the Payment Date immediately preceding the Amortization Date. Borrower agrees to pay, on the Funding Date of each Term Loan, any initial partial monthly interest payment otherwise due for the period between the Funding Date of such Term Loan and the first Payment Date thereof. Commencing on the Amortization Date, and continuing on the Payment Date of each month thereafter, Borrower shall make consecutive equal monthly payments of principal, together with applicable interest, in arrears, to each Lender, as calculated by Collateral Agent (which calculations shall be deemed correct absent manifest error) based upon: (1) the amount of such Lender's Term Loan, (2) the effective rate of interest, as determined in Section 2.3(a), and (3) a repayment schedule equal to thirty-six (36) months if the Amortization Date is December 1, 2017 or thirty (30) months if the Amortization Date is June 1, 2018. All unpaid principal and accrued and unpaid interest with respect to each Term Loan is due and payable in full on the Maturity Date. Each Term Loan may only be prepaid in accordance with Sections 2.2(c) and 2.2(d).

(c) Mandatory Prepayments. If the Term Loans are accelerated following the occurrence of an Event of Default, Borrower shall immediately pay to Lenders, payable to each Lender in accordance with its respective Pro Rata Share, an amount equal to the sum of: (i) all outstanding principal of the Term Loans plus accrued and unpaid interest thereon through the prepayment date, (ii) the Final Payment, (iii) the Prepayment Fee, (iv) the Term B Loan Non-Usage Fee, (v) the Term C Loan Non-Usage Fee, plus (v) all other Obligations that are due and payable, including Lenders' Expenses and interest at the Default Rate with respect to any past due amounts. Notwithstanding (but without duplication with) the foregoing, on the Maturity Date, if the Final Payment had not previously been paid in full in connection with the prepayment of the Term Loans in full, Borrower shall pay to Collateral Agent, for payment to each Lender in accordance with its respective Pro Rata Share, the Final Payment in respect of the Term Loan(s).

(d) Permitted Prepayment of Term Loans. Borrower shall have the option to prepay all, but not less than all, of the Term Loans advanced by the Lenders under this Agreement, provided Borrower (i) provides written notice to Collateral Agent of its election to prepay the Term Loans at least five (5) Business Days prior to such prepayment, and (ii) pays to the Lenders on the date of such prepayment, payable to each Lender in accordance with its respective Pro Rata Share, an amount equal to the sum of (A) all outstanding principal of the Term Loans plus accrued and unpaid interest thereon through the prepayment date, (B) the Final Payment, (C) the Prepayment Fee, (D) the Term B Loan Non-Usage Fee, (E) the Term C Loan Non-Usage Fee, plus (F) all other Obligations that are due and payable, including Lenders' Expenses and interest at the Default Rate with respect to any past due amounts.

2.3 Payment of Interest on the Credit Extensions.

(a) Interest Rate. Subject to Section 2.3(b), the principal amount outstanding under the Term Loans shall accrue interest at a floating per annum rate equal to the Basic Rate, determined by Collateral Agent on the Funding Date of the applicable Term Loan, which interest shall be payable monthly in arrears in accordance with Sections 2.2(b) and 2.3(e). Interest shall accrue on each Term Loan commencing on, and including, the Funding Date of such Term Loan, and shall accrue on the principal amount outstanding under such Term Loan through and including the day on which such Term Loan is paid in full.

(b) Default Rate. Immediately upon the occurrence and during the continuance of an Event of Default, outstanding principal and interest shall accrue interest at a floating per annum rate equal to the rate that is otherwise applicable thereto plus five percentage points (5.00%) (the "**Default Rate**") unless Collateral Agent at the direction of the Required Lenders elects from time to time in its sole discretion to impose a smaller increase. Payment or acceptance of the increased interest rate provided in this Section 2.3(b) is not a permitted alternative to timely payment and shall not constitute a waiver of any Event of Default or otherwise prejudice or limit any rights or remedies of Collateral Agent.

(c) 360-Day Year. Interest shall be computed on the basis of a three hundred sixty (360) day year, and the actual number of days elapsed.

(d) Debit of Accounts. Collateral Agent and each Lender may debit (or ACH) any deposit accounts, maintained by Borrower or any of its Subsidiaries, including the Designated Deposit Account, for

principal and interest payments or any other amounts Borrower owes the Lenders under the Loan Documents when due and owing. Collateral Agent shall promptly notify Borrower when it debits Borrower's accounts. Any such debits (or ACH activity) shall not constitute a set-off.

(e) Payments. Except as otherwise expressly provided herein, all payments by Borrower under the Loan Documents shall be made to the respective Lender to which such payments are owed, at such Lender's office in immediately available funds on the date specified herein. Unless otherwise provided, interest is payable monthly on the Payment Date of each month. Payments of principal and/or interest received after 12:00 noon Eastern time are considered received at the opening of business on the next Business Day. When a payment is due on a day that is not a Business Day, the payment is due the next Business Day and additional fees or interest, as applicable, shall continue to accrue until paid. All payments to be made by Borrower hereunder or under any other Loan Document, including payments of principal and interest, and all fees, expenses, indemnities and reimbursements, shall be made without set-off, recoupment or counterclaim, in lawful money of the United States and in immediately available funds.

2.4 Secured Promissory Notes. If requested by a Lender, the Term Loans advanced by such Lender shall be evidenced by a Secured Promissory Note or Notes in the form attached as Exhibit D hereto (each a "**Secured Promissory Note**"), and shall be repayable as set forth in this Agreement. Borrower irrevocably authorizes each Lender to make or cause to be made, on or about the Funding Date of any Term Loan or at the time of receipt of any payment of principal on such Lender's Secured Promissory Note, an appropriate notation on such Lender's Secured Promissory Note Record reflecting the making of such Term Loan or (as the case may be) the receipt of such payment. The outstanding amount of each Term Loan set forth on such Lender's Secured Promissory Note Record shall be prima facie evidence of the principal amount thereof owing and unpaid to such Lender, but the failure to record, or any error in so recording, any such amount on such Lender's Secured Promissory Note Record shall not limit or otherwise affect the obligations of Borrower under any Secured Promissory Note or any other Loan Document to make payments of principal of or interest on any Secured Promissory Note when due. Upon receipt of an affidavit of an officer of a Lender as to the loss, theft, destruction, or mutilation of its Secured Promissory Note**,** Borrower shall issue, in lieu thereof, a replacement Secured Promissory Note in the same principal amount thereof in the form attached as Exhibit D hereto.

2.5 Fees. Borrower shall pay to Collateral Agent:

(a) Facility Fee. A fully earned, non-refundable facility fee equal to one percent (1.00%) of each Term Loan to be shared between the Lenders pursuant to their respective Pro Rata Shares due and payable on the Funding Date of such Term Loan;

(b) Final Payment. The Final Payment, when due hereunder, to be shared between the Lenders in accordance with their respective Pro Rata Shares;

(c) Prepayment Fee. The Prepayment Fee, when due hereunder, to be shared between the Lenders in accordance with their respective Pro Rata Shares;

(d) Term B Loan Non-Usage Fee. The Term B Loan Non-Usage Fee, when due hereunder, to be shared between the Lenders in accordance with their respective Pro Rata Shares;

(e) Term C Loan Non-Usage Fee. The Term C Loan Non-Usage Fee, when due hereunder, to be shared between the Lenders in accordance with their respective Pro Rata Shares; and

(f) Lenders' Expenses. All Lenders' Expenses (including reasonable documented out-of-pocket attorneys' fees and expenses for documentation and negotiation of this Agreement incurred through and after the Effective Date, when due.

2.6 Withholding. Payments received by the Lenders from Borrower hereunder will be made free and clear of and without deduction for any and all present or future taxes, levies, imposts, duties, deductions, withholdings, assessments, fees or other charges imposed by any governmental authority (including any interest, additions to tax or penalties applicable thereto). Specifically, however, if at any time any Governmental Authority, applicable law, regulation or international agreement requires Borrower to make any withholding or deduction from

any such payment or other sum payable hereunder to the Lenders, Borrower hereby covenants and agrees that the amount due from Borrower with respect to such payment or other sum payable hereunder will be increased to the extent necessary to ensure that, after the making of such required withholding or deduction, each Lender receives a net sum equal to the sum which it would have received had no withholding or deduction been required and Borrower shall pay the full amount withheld or deducted to the relevant Governmental Authority; provided, however, that to the extent a Lender is refunded any portion of such excess, such Lender shall remit such amount of Borrower. Borrower will, upon request, furnish the Lenders with proof reasonably satisfactory to the Lenders indicating that Borrower has made such withholding payment; provided, however, that Borrower need not make any withholding payment if the amount or validity of such withholding payment is contested in good faith by appropriate and timely proceedings and as to which payment in full is bonded or reserved against by Borrower. The agreements and obligations of Borrower contained in this Section 2.6 shall survive the termination of this Agreement.

3. CONDITIONS OF LOANS

3.1 Conditions Precedent to Initial Credit Extension. Each Lender's obligation to make a Term A Loan is subject to the condition precedent that Collateral Agent and each Lender shall consent to or shall have received, in form and substance satisfactory to Collateral Agent and each Lender, such documents, and completion of such other matters, as Collateral Agent and each Lender may reasonably request, including, without limitation:

(a) original Loan Documents, each duly executed by Borrower and each Subsidiary which is a guarantor, as applicable;

(b) duly executed original Control Agreements with respect to any Collateral Accounts maintained by Borrower or any of its Subsidiaries that are guarantors;

(c) to the extent requested, duly executed original Secured Promissory Notes in favor of each Lender according to its Term Loan Commitment Percentage;

(d) the Operating Documents and good standing certificates of Borrower and its Subsidiaries that are guarantors certified by the Secretary of State (or equivalent agency) of Borrower's and such Subsidiaries' jurisdiction of organization or formation and each jurisdiction in which Borrower and each Subsidiary that is a guarantor is qualified to conduct business, each as of a date no earlier than thirty (30) days prior to the Effective Date;

(e) a completed Perfection Certificate for Borrower and each of its Subsidiaries;

(f) the Annual Projections, for the current calendar year;

(g) duly executed original officer's certificate for Borrower and each Subsidiary that is a party to the Loan Documents, in a form reasonably acceptable to Collateral Agent and the Lenders;

(h) certified copies, dated as of date no earlier than thirty (30) days prior to the Effective Date, of financing statement searches, as Collateral Agent shall request, accompanied by written evidence (including any UCC termination statements) that the Liens indicated in any such financing statements either constitute Permitted Liens or have been or, in connection with the initial Credit Extension, will be terminated or released;

(i) a landlord's consent executed in favor of Collateral Agent in respect of all of Borrower's leased location at 3545-3575 John Hopkins Court, San Diego, CA 92121;

(j) a bailee waiver executed in favor of Collateral Agent in respect of each third party bailee where Borrower or any Subsidiary maintains Collateral having a book value in excess of Two Hundred Fifty Thousand Dollars ($250,000.00);

(k) a duly executed legal opinion of counsel to Borrower dated as of the Effective Date;

(l) evidence satisfactory to Collateral Agent and the Lenders that the insurance policies required by Section 6.5 hereof are in full force and effect, together with appropriate evidence showing loss payable and/or additional insured clauses or endorsements in favor of Collateral Agent, for the ratable benefit of the Lenders;

(m) a payoff letter from SVB in respect of the Existing Indebtedness;

(n) evidence that (i) the Liens securing the Existing Indebtedness will be terminated and (ii) the documents and/or filings evidencing the perfection of such Liens, including without limitation any financing statements and/or control agreements, have or will, concurrently with the initial Credit Extension, be terminated;

(o) payment of the fees and Lenders' Expenses then due as specified in Section 2.5 hereof.

3.2 Conditions Precedent to all Credit Extensions. The obligation of each Lender to make each Credit Extension, including the initial Credit Extension, is subject to the following conditions precedent:

(a) receipt by (i) the Lenders of an executed Disbursement Letter in the form of Exhibit B-1 attached hereto; and (ii) SVB of an executed Loan Payment/Advance Request Form in the form of Exhibit B-2 attached hereto;

(b) the representations and warranties in Section 5 hereof shall be true and correct in all material respects on the date of the Disbursement Letter (and the Loan Payment/Advance Request Form) and on the Funding Date of each Credit Extension; provided, however, that such materiality qualifier shall not be applicable to any representations and warranties that already are qualified or modified by materiality in the text thereof; and provided, further that those representations and warranties expressly referring to a specific date shall be true and correct in all material respects as of such date, and no Event of Default shall have occurred and be continuing or immediately result from the Credit Extension. Each Credit Extension is Borrower's representation and warranty on that date that the representations and warranties in Section 5 hereof are true and correct in all material respects as of such date; provided, however, that such materiality qualifier shall not be applicable to any representations and warranties that already are qualified or modified by materiality in the text thereof; and provided, further that those representations and warranties expressly referring to a specific date shall be true and correct in all material respects as of such date;

(c) in Collateral Agent's and each Required Lender's reasonable discretion, there has not been any Material Adverse Change or any material adverse deviation by Borrower from the Annual Projections of Borrower presented to and accepted by Collateral Agent and each Required Lender;

(d) to the extent not delivered at the Effective Date, duly executed original Secured Promissory Notes (if requested by a Lender) and Warrants in form and substance substantially consistent with the Warrants delivered on the Effective Date in favor of each Lender according to its Commitment Percentage, with respect to each Credit Extension made by such Lender after the Effective Date; and

(e) payment of the fees and Lenders' Expenses then due as specified in Section 2.5 hereof.

3.3 Covenant to Deliver. Borrower agrees to deliver to Collateral Agent and the Lenders each item required to be delivered to Collateral Agent under this Agreement as a condition precedent to any Credit Extension. Borrower expressly agrees that a Credit Extension made prior to the receipt by Collateral Agent or any Lender of any such item shall not constitute a waiver by Collateral Agent or any Lender of Borrower's obligation to deliver such item, and any such Credit Extension in the absence of a required item shall be made in each Lender's sole discretion.

3.4 Procedures for Borrowing. Subject to the prior satisfaction of all other applicable conditions to the making of a Term Loan set forth in this Agreement, to obtain a Term Loan, Borrower shall notify the Lenders (which notice shall be irrevocable) by electronic mail, facsimile, or telephone by 3:00 p.m. Eastern time three (3) Business Days prior to the date the Term Loan is to be made. Together with any such electronic, facsimile or telephonic notification, Borrower shall deliver to the Lenders by electronic mail or facsimile a completed Disbursement Letter (and the Loan Payment/Advance Request Form, with respect to SVB) executed by a Responsible Officer or his or her designee. The Lenders may rely on any telephone notice given by a person whom

* Confidential information, indicated [***], has been omitted from this filing and filed separately with the Securities and Exchange Commission.

a Lender reasonably believes is a Responsible Officer or designee. On the Funding Date, each Lender shall credit and/or transfer (as applicable) to the Designated Deposit Account, an amount equal to its Term Loan Commitment.

4. CREATION OF SECURITY INTEREST

4.1 Grant of Security Interest. Borrower hereby grants Collateral Agent, for the ratable benefit of the Lenders, to secure the payment and performance in full of all of the Obligations, a continuing security interest in, and pledges to Collateral Agent, for the ratable benefit of the Lenders, the Collateral, wherever located, whether now owned or hereafter acquired or arising, and all proceeds and products thereof. Borrower represents, warrants, and covenants that the security interest granted herein is and shall at all times continue to be a first priority perfected security interest in the Collateral, subject only to Permitted Liens that are permitted by the terms of this Agreement to have priority to Collateral Agent's Lien. If Borrower shall acquire a commercial tort claim (as defined in the Code) in excess of Fifty Thousand Dollars ($50,000.00), Borrower, shall promptly notify Collateral Agent in a writing signed by Borrower, as the case may be, of the general details thereof (and further details as may be required by Collateral Agent) and grant to Collateral Agent, for the ratable benefit of the Lenders, in such writing a security interest therein and in the proceeds thereof, all upon the terms of this Agreement, with such writing to be in form and substance reasonably satisfactory to Collateral Agent.

Borrower acknowledges that it previously has entered, and/or may in the future enter, into Bank Services Agreements with Bank. Regardless of the terms of any Bank Services Agreement, Borrower agrees that any amounts Borrower owes Bank thereunder shall be deemed to be Obligations hereunder and that it is the intent of Borrower and Bank to have all such Obligations secured by the first priority perfected security interest in the Collateral granted herein (subject only to Permitted Liens that may have superior priority to Bank's Lien in this Agreement).

If this Agreement is terminated, Collateral Agent's Lien in the Collateral shall continue until the Obligations (other than inchoate indemnity or reimbursement obligations or other obligations which, by their terms, survive the termination of this Agreement) are repaid in full in cash. Upon payment in full in cash of the Obligations (other than inchoate indemnity or reimbursement obligations or other obligations which, by their terms, survive the termination of this Agreement) and at such time as the Lenders' obligation to make Credit Extensions has terminated, Collateral Agent shall, at the sole cost and expense of Borrower, release its Liens in the Collateral and all rights therein shall revert to Borrower. In the event (x) all Obligations (other than inchoate indemnity or reimbursement obligations or other obligations which, by their terms, survive the termination of this Agreement), except for Bank Services, are satisfied in full, and (y) this Agreement is terminated, Bank shall terminate the security interest granted herein upon Borrower providing cash collateral acceptable to Bank in its good faith business judgment for Bank Services, if any. In the event such Bank Services consist of outstanding Letters of Credit, Borrower shall provide to Bank cash collateral in an amount equal to (x) if such Letters of Credit are denominated in Dollars, then one hundred five percent (105%); and (y) if such Letters of Credit are denominated in a Foreign Currency, then one hundred ten percent (110%), of the Dollar Equivalent of the face amount of all such Letters of Credit plus all interest, fees, and costs due or to become due in connection therewith (as estimated by Bank in its good faith business judgment), to secure all of the Obligations relating to such Letters of Credit.

4.2 Authorization to File Financing Statements. Borrower hereby authorizes Collateral Agent to file financing statements or take any other action required to perfect Collateral Agent's security interests in the Collateral, without notice to Borrower (except to the extent notice to Borrower is required, as determined by Collateral Agent, in order for Collateral Agent to perfect its security interest in such Collateral), with all appropriate jurisdictions to perfect or protect Collateral Agent's interest or rights under the Loan Documents, including a notice that any disposition of the Collateral, except to the extent permitted by the terms of this Agreement, by Borrower, or any other Person, shall be deemed to violate the rights of Collateral Agent under the Code.

4.3 Pledge of Collateral. Borrower hereby pledges, collaterally assigns and grants to Collateral Agent, for the ratable benefit of the Lenders, a security interest in all the Shares, together with all proceeds and substitutions thereof, all cash, stock and other moneys and property paid thereon, all rights to subscribe for securities declared or granted in connection therewith, and all other cash and noncash proceeds of the foregoing, as security for the performance of the Obligations. On the Effective Date, or, to the extent not certificated as of the Effective Date, within ten (10) days of the certification of any Shares, the certificate or certificates for the Shares will be delivered to Collateral Agent, accompanied by an instrument of assignment duly executed in blank by Borrower. To

the extent required by the terms and conditions governing the Shares, Borrower shall cause the books of each entity whose Shares are part of the Collateral and any transfer agent to reflect the pledge of the Shares. Upon the occurrence and during the continuance of an Event of Default hereunder, Collateral Agent may effect the transfer of any securities included in the Collateral (including but not limited to the Shares) into the name of Collateral Agent and cause new (as applicable) certificates representing such securities to be issued in the name of Collateral Agent or its transferee. Borrower will execute and deliver such documents, and take or cause to be taken such actions, as Collateral Agent may reasonably request to perfect or continue the perfection of Collateral Agent's security interest in the Shares. Unless an Event of Default shall have occurred and be continuing, Borrower shall be entitled to exercise any voting rights with respect to the Shares and to give consents, waivers and ratifications in respect thereof, provided that no vote shall be cast or consent, waiver or ratification given or action taken which would be inconsistent with any of the terms of this Agreement or which would constitute or create any violation of any of such terms. All such rights to vote and give consents, waivers and ratifications shall terminate upon the occurrence and continuance of an Event of Default. Collateral Agent reserves the right to take such steps as may be necessary to perfect a Lien in the Shares of Pangu.

5. REPRESENTATIONS AND WARRANTIES

Borrower represents and warrants to Collateral Agent and the Lenders as follows:

5.1 Due Organization, Authorization: Power and Authority. Borrower and each of its Subsidiaries is duly existing and in good standing as a Registered Organization in its jurisdictions of organization or formation and Borrower and each of its Subsidiaries is qualified and licensed to do business and is in good standing in any jurisdiction in which the conduct of its businesses or its ownership of property requires that it be qualified except where the failure to do so could not reasonably be expected to have a Material Adverse Change. In connection with this Agreement, Borrower and each of its Subsidiaries has delivered to Collateral Agent a completed perfection certificate signed by an officer of Borrower or such Subsidiary (each a "**Perfection Certificate**" and collectively, the "**Perfection Certificates**"). Borrower represents and warrants that (a) Borrower and each of its Subsidiaries' exact legal name is that which is indicated on its respective Perfection Certificate and on the signature page of each Loan Document to which it is a party; (b) Borrower and each of its Subsidiaries is an organization of the type and is organized in the jurisdiction set forth on its respective Perfection Certificate; (c) each Perfection Certificate accurately sets forth each of Borrower's and its Subsidiaries' organizational identification number or accurately states that Borrower or such Subsidiary has none; (d) each Perfection Certificate accurately sets forth Borrower's and each of its Subsidiaries' place of business, or, if more than one, its chief executive office as well as Borrower's and each of its Subsidiaries' mailing address (if different than its chief executive office); (e) Borrower and each of its Subsidiaries (and each of its respective predecessors) have not, in the past five (5) years, changed its jurisdiction of organization, organizational structure or type, or any organizational number assigned by its jurisdiction; and (f) all other information set forth on the Perfection Certificates pertaining to Borrower and each of its Subsidiaries, is accurate and complete (it being understood and agreed that Borrower and each of its Subsidiaries may from time to time update certain information in the Perfection Certificates (including the information set forth in clause (d) above) after the Effective Date to the extent permitted by one or more specific provisions in this Agreement); such updated Perfection Certificates subject to the review and approval of Collateral Agent. If Borrower or any of its Subsidiaries is not now a Registered Organization but later becomes one, Borrower shall notify Collateral Agent of such occurrence and provide Collateral Agent with such Person's organizational identification number within five (5) Business Days of receiving such organizational identification number.

The execution, delivery and performance by Borrower and each of its Subsidiaries of the Loan Documents to which it is a party have been duly authorized, and do not (i) conflict with any of Borrower's or such Subsidiaries' organizational documents, including its respective Operating Documents, (ii) contravene, conflict with, constitute a default under or violate any material Requirement of Law applicable thereto, (iii) contravene, conflict or violate any applicable order, writ, judgment, injunction, decree, determination or award of any Governmental Authority by which Borrower or such Subsidiary, or any of their property or assets may be bound or affected, except as could not reasonably be expected to have a Material Adverse Effect, (iv) require any action by, filing, registration, or qualification with, or Governmental Approval from, any Governmental Authority (except such Governmental Approvals which have already been obtained and are in full force and effect) or are being obtained pursuant to Section 6.1(b) or which the failure to obtain could not reasonably be expected to result in a Material Adverse Effect, or (v) constitute an event of default under any material agreement by which Borrower or any of such Subsidiaries, or their respective properties, is bound. Neither Borrower nor any of its Subsidiaries is in default under any agreement

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to which it is a party or by which it or any of its assets is bound in which such default could reasonably be expected to have a Material Adverse Change.

5.2 Collateral.

(a) Borrower and each its Subsidiaries have good title to, have rights in, and the power to transfer each item of the Collateral upon which it purports to grant a Lien under the Loan Documents, free and clear of any and all Liens except Permitted Liens, and neither Borrower nor any of its Subsidiaries have any Deposit Accounts, Securities Accounts, Commodity Accounts or other investment accounts other than the Collateral Accounts or the other investment accounts, if any, described in the Perfection Certificates delivered to Collateral Agent in connection herewith with respect of which Borrower or such Subsidiary has given Collateral Agent notice and taken such actions as are necessary to give Collateral Agent a perfected security interest therein (to the extent required pursuant to the terms of Section 6.6(b)). The Accounts are bona fide, existing obligations of the Account Debtors.

(b) On the Effective Date, and except as disclosed on the Perfection Certificate, no Collateral with a book value in excess of Two Hundred Fifty Thousand Dollars ($250,000.00) is in the possession of any third party bailee (such as a warehouse), other than pre-commercial drug substances and products and pre-filled syringes for clinical trials having a book value not in excess of Two Hundred Fifty Thousand Dollars ($250,000.00) in the aggregate. None of the components of the Collateral shall be maintained at locations other than as disclosed in the Perfection Certificates on the Effective Date or locations which Borrower notifies Collateral Agent and each Lender of in writing from time to time in accordance with this Agreement.

(c) All Inventory is in all material respects of good and marketable quality, free from material defects.

(d) Borrower and each of its Subsidiaries is the sole owner of the Intellectual Property each respectively purports to own, free and clear of all Liens other than Permitted Liens except for (a) non-exclusive licenses granted to its customers in the ordinary course of business, (b) over-the-counter software that is commercially available to the public, and (c) Intellectual Property licensed to Borrower. Except as noted on the Perfection Certificates, neither Borrower nor any of its Subsidiaries is a party to, nor is bound by, any material license or other material agreement with respect to which Borrower or such Subsidiary is the licensee that (i) prohibits or otherwise restricts Borrower or its Subsidiaries from granting a security interest in Borrower's or such Subsidiaries' interest in such material license or other material agreement or any other property, or (ii) for which a default under or termination of could interfere with Collateral Agent's or any Lender's right to sell any Collateral. Borrower shall provide written notice to Collateral Agent and each Lender within ten (10) days of Borrower or any of its Subsidiaries entering into or becoming bound by any license or agreement with respect to which Borrower or any Subsidiary is the licensee (other than over-the-counter software that is commercially available to the public) which prohibits or otherwise restricts Borrower or its Subsidiaries from granting a security interest in Borrower's or such Subsidiaries' interest in such material license).

5.3 Litigation. Except as disclosed (i) on the Perfection Certificates, or (ii) in accordance with Section 6.9 hereof, there are no actions, suits, investigations (to Borrower's knowledge), or proceedings pending or, to the knowledge of the Responsible Officers, threatened in writing by or against Borrower or any of its Subsidiaries involving more than Two Hundred Fifty Thousand Dollars ($250,000.00).

5.4 No Material Deterioration in Financial Condition; Financial Statements. All consolidated financial statements for Borrower and its Subsidiaries, delivered to Collateral Agent fairly present, in conformity with GAAP, in all material respects the consolidated financial condition of Borrower and its Subsidiaries, and the consolidated results of operations as of the date hereof of Borrower and its Subsidiaries, except that unaudited financial statements may be subject to normal year-end adjustments and may not contain adjustments for stock compensation or footnotes. There has not been any material deterioration in the consolidated financial condition of Borrower and its Subsidiaries since the date of the most recent financial statements submitted to any Lender.

5.5 Solvency. Borrower is, and Borrower and each of its Subsidiaries, taken as a whole on a consolidated basis, are Solvent.

5.6 Regulatory Compliance. Neither Borrower nor any of its Subsidiaries is an "investment company" or a company "controlled" by an "investment company" under the Investment Company Act of 1940, as amended. Neither Borrower nor any of its Subsidiaries is engaged as one of its important activities in extending credit for margin stock (under Regulations X, T and U of the Federal Reserve Board of Governors). Borrower and each of its Subsidiaries has complied in all material respects with applicable provisions of the Federal Fair Labor Standards Act. Neither Borrower nor any of its Subsidiaries is a "holding company" or an "affiliate" of a "holding company" or a "subsidiary company" of a "holding company" as each term is defined and used in the Public Utility Holding Company Act of 2005. Neither Borrower nor any of its Subsidiaries has violated any laws, ordinances or rules, the violation of which could reasonably be expected to have a Material Adverse Change. Neither Borrower's nor any of its Subsidiaries' properties or assets has been used by Borrower or such Subsidiary or, to Borrower's knowledge, by previous Persons, in disposing, producing, storing, treating, or transporting any hazardous substance other than in material compliance with applicable laws. Borrower and each of its Subsidiaries has obtained all consents, approvals and authorizations of, made all declarations or filings with, and given all notices to, all Governmental Authorities that are necessary to continue their respective businesses as currently conducted.

None of Borrower, any of its Subsidiaries, or any of Borrower's or its Subsidiaries' Affiliates or any of their respective agents acting or benefiting in any capacity in connection with the transactions contemplated by this Agreement is (i) in violation of any Anti-Terrorism Law, (ii) engaging in or conspiring to engage in any transaction that evades or avoids, or has the purpose of evading or avoiding or attempts to violate, any of the prohibitions set forth in any Anti-Terrorism Law, or (iii) is a Blocked Person. None of Borrower, any of its Subsidiaries, or to the knowledge of Borrower and any of their Affiliates or agents, acting or benefiting in any capacity in connection with the transactions contemplated by this Agreement, (x) conducts any business or engages in making or receiving any contribution of funds, goods or services to or for the benefit of any Blocked Person, or (y) deals in, or otherwise engages in any transaction relating to, any property or interest in property blocked pursuant to Executive Order No. 13224, any similar executive order or other Anti-Terrorism Law.

5.7 Investments. Neither Borrower nor any of its Subsidiaries owns any stock, shares, partnership interests or other equity securities except for Permitted Investments.

5.8 Tax Returns and Payments; Pension Contributions. Borrower and each of its Subsidiaries has timely filed all required tax returns and reports, and Borrower and each of its Subsidiaries, has timely paid all foreign, federal, state, and local taxes, assessments, deposits and contributions owed by Borrower and such Subsidiaries, in all jurisdictions in which Borrower or any such Subsidiary is subject to taxes, including the United States, unless such taxes are being contested in accordance with the following sentence. Borrower and each of its Subsidiaries, may defer payment of any contested taxes, provided that Borrower or such Subsidiary, (a) in good faith contests its obligation to pay the taxes by appropriate proceedings promptly and diligently instituted and conducted, (b) notifies Collateral Agent in writing of the commencement of, and any material development in, the proceedings, and (c) posts bonds or takes any other steps required to prevent the Governmental Authority levying such contested taxes from obtaining a Lien upon any of the Collateral that is other than a "**Permitted Lien**." Neither Borrower nor any of its Subsidiaries is aware of any claims or adjustments proposed for any of Borrower's or such Subsidiaries', prior tax years which could result in additional taxes becoming due and payable by Borrower or its Subsidiaries. Borrower and each of its Subsidiaries have paid all amounts necessary to fund all present pension, profit sharing and deferred compensation plans in accordance with their terms, and neither Borrower nor any of its Subsidiaries have, withdrawn from participation in, and have not permitted partial or complete termination of, or permitted the occurrence of any other event with respect to, any such plan which could reasonably be expected to result in any liability of Borrower or its Subsidiaries, including any liability to the Pension Benefit Guaranty Corporation or its successors or any other Governmental Authority.

5.9 Use of Proceeds. Borrower shall use the proceeds of the Credit Extensions solely as working capital and to fund its general business requirements, and not for personal, family, household or agricultural purposes. A portion of the proceeds of the Term A Loans shall be used by Borrower to repay the Existing Indebtedness in full on the Effective Date.

5.10 Shares. Borrower has full power and authority to create a first lien on the Shares and no disability or contractual obligation exists that would prohibit Borrower from pledging the Shares pursuant to this Agreement. To Borrower's knowledge, there are no subscriptions, warrants, rights of first refusal or other restrictions on transfer relative to, or options exercisable with respect to the Shares (other than pursuant to the Loan Documents). The

Shares have been and will be duly authorized and validly issued, and are fully paid and non-assessable. To Borrower's knowledge, the Shares are not the subject of any suit, action, arbitration, administrative or other proceeding (in each case, present or threatened in writing), and Borrower knows of no reasonable grounds for the institution of any such proceedings.

5.11 Full Disclosure. No written representation, warranty or other statement of Borrower or any of its Subsidiaries in any certificate or written statement given to Collateral Agent or any Lender, as of the date such representation, warranty, or other statement was made, taken together with all such written certificates and written statements given to Collateral Agent or any Lender, contains any untrue statement of a material fact or omits to state a material fact necessary to make the statements contained in the certificates or statements not misleading in light of the circumstances under which they were made (it being recognized that the projections and forecasts provided by Borrower in good faith and based upon reasonable assumptions are not viewed as facts and that actual results during the period or periods covered by such projections and forecasts may differ from the projected or forecasted results).

5.12 Definition of "Knowledge." For purposes of the Loan Documents, whenever a representation or warranty is made to Borrower's knowledge or awareness, to the "best of" Borrower's knowledge, or with a similar qualification, knowledge or awareness means the actual knowledge, after reasonable investigation, of the Responsible Officers.

6. AFFIRMATIVE COVENANTS

Borrower shall, and shall cause each of its Subsidiaries, as applicable, to, do all of the following:

6.1 Government Compliance.

(a) Maintain its and (except as permitted under Section 7.3) all its Subsidiaries' legal existence and good standing in their respective jurisdictions of organization and maintain qualification in each jurisdiction in which the failure to so qualify could reasonably be expected to have a Material Adverse Change. Comply with all laws, ordinances and regulations to which Borrower or any of its Subsidiaries is subject, the noncompliance with which could reasonably be expected to have a Material Adverse Change.

(b) Obtain and keep in full force and effect, all of the material Governmental Approvals necessary for the performance by Borrower and its Subsidiaries of their respective businesses and obligations under the Loan Documents and the grant of a security interest to Collateral Agent for the ratable benefit of the Lenders, in all of the Collateral. Borrower shall promptly provide copies to Collateral Agent of any material Governmental Approvals obtained by Borrower or any of its Subsidiaries.

6.2 Financial Statements, Reports, Certificates.

(a) Deliver to Collateral Agent and each Required Lender:

(i) as soon as available, but no later than five (5) days after filing with the SEC, a company prepared consolidated and consolidating (to the extent prepared) balance sheet, income statement and cash flow statement covering the consolidated operations of Borrower and its Subsidiaries for such quarter certified by a Responsible Officer and in a form reasonably acceptable to Collateral Agent and each Lender;

(ii) as soon as available, but no later than the earlier of (A) one hundred eighty (180) days after the last day of Borrower's fiscal year or (B) five (5) days after filing with the SEC, audited consolidated financial statements prepared under GAAP, consistently applied, together with an unqualified opinion (other than as to going concern or a qualification resulting solely from the schedule maturity of the Term Loans occurring within one year from the date such opinion is delivered) on the financial statements from Ernst & Young, any "Big Four" accounting firm, and an independent certified public accounting firm acceptable to Collateral Agent in their reasonable discretion**;**

(iii) as soon as available after approval thereof by Borrower's Board of Directors, but no later than the earlier of (A) sixty (60) days after the last day of each of Borrower's fiscal years or (B) seven (7) days after approved by Borrower's Board of Directors, Borrower's annual financial projections for the entire

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current fiscal year as approved by Borrower's Board of Directors, which such annual financial projections shall be set forth in a quarter-by-quarter format (such annual financial projections as originally delivered to Collateral Agent and the Lenders are referred to herein as the "**Annual Projections**"; provided that, any revisions of the Annual Projections approved by Borrower's Board of Directors shall be delivered to Collateral Agent and the Lenders no later than seven (7) days after such approval);

(iv) within five (5) days of delivery, copies of all statements, reports and notices made generally available to Borrower's security holders or holders of Subordinated Debt;

(v) in the event that Borrower becomes subject to the reporting requirements under the Securities Exchange Act of 1934, as amended, within five (5) days of filing, all reports on Form 10-K, 10-Q and 8-K filed with the Securities and Exchange Commission;

(vi) prompt notice of any event that could reasonably be expected to materially and adversely affect the value of the Intellectual Property;

(vii) as soon as available, but no later than thirty (30) days after the last day of each month, copies of the month-end account statements for each Collateral Account maintained by Borrower or its Subsidiaries, which statements may be provided to Collateral Agent and each Required Lender by Borrower or directly from the applicable institution(s), and

(viii) other information as reasonably requested by Collateral Agent or any Lender.

Notwithstanding the foregoing, documents required to be delivered pursuant to the terms hereof (to the extent any such documents are included in materials otherwise filed with the SEC) may be delivered electronically and if so delivered, shall be deemed to have been delivered on the date on which Borrower posts such documents, or provides a link thereto, on Borrower's website on the internet at Borrower's website address.

(b) Concurrently with the delivery of the financial statements specified in Section 6.2(a)(i) above but no later than five (5) days after filing the financial statements specified in Section 6.2(a)(i) above with the SEC, deliver to each Lender, a duly completed Compliance Certificate signed by a Responsible Officer.

(c) Keep proper books of record and account in accordance with GAAP in all material respects, in which full, true and correct entries shall be made of all dealings and transactions in relation to its business and activities. Borrower shall, and shall cause each of its Subsidiaries to, allow, at the sole cost of Borrower, Collateral Agent or any Lender, during regular business hours upon reasonable prior notice (provided that no notice shall be required when an Event of Default has occurred and is continuing), to visit and inspect any of its properties, to examine and make abstracts or copies from any of its books and records, and to conduct a collateral audit and analysis of its operations and the Collateral. Such audits shall be conducted no more often than once every calendar year unless (and more frequently if) an Event of Default has occurred and is continuing.

6.3 Inventory; Returns. Keep all Inventory in good and marketable condition (ordinary wear and tear excepted), free from material defects. Returns and allowances between Borrower, or any of its Subsidiaries, and their respective Account Debtors shall follow Borrower's, or such Subsidiary's, customary practices. Borrower must promptly notify Collateral Agent and the Required Lenders of all returns, recoveries, disputes and claims that involve more than One Hundred Thousand Dollars ($100,000.00) individually or in the aggregate in any calendar year.

6.4 Taxes; Pensions. Timely file and require each of its Subsidiaries to timely file, all required tax returns and reports required to be filed by Borrower or such Subsidiary and timely pay, and require each of its Subsidiaries to timely file, all foreign, federal, state, and local taxes, assessments, deposits and contributions owed by Borrower or its Subsidiaries, except for deferred payment of any taxes contested pursuant to the terms of Section 5.8 hereof, and shall deliver to Lenders, on reasonable request, appropriate certificates attesting to such payments, and pay all amounts necessary to fund all present pension, profit sharing and deferred compensation plans in accordance with the terms of such plans.

6.5 Insurance. Keep Borrower's and its Subsidiaries' business and the Collateral insured for risks and in amounts customary for companies of Borrower's size in Borrower's and its Subsidiaries' industry and location. Insurance policies shall be in a form, with companies, and in amounts that are reasonably satisfactory to Collateral Agent and Lenders (it being acknowledged and agreed by Collateral Agent and Lenders that the insurance maintained by Borrower and its Subsidiaries as of the date hereof is satisfactory). All property policies shall have a lender's loss payable endorsement showing Collateral Agent as lender loss payee and waive subrogation against Collateral Agent, and all liability policies shall show, or have endorsements showing, Collateral Agent, as additional insured. The Collateral Agent shall be named as lender loss payee and/or additional insured with respect to any such insurance providing coverage in respect of any Collateral, and each provider of any such insurance shall agree, by endorsement upon the policy or policies issued by it or by independent instruments furnished to the Collateral Agent, that it will give the Collateral Agent thirty (30) days prior written notice before any such policy or policies shall be materially altered or canceled; provided that in the event such provider does not agree to give notice of material alteration, Borrower shall give Collateral Agent such 30 days' prior notice. At Collateral Agent's request, Borrower shall deliver certified copies of policies and evidence of all premium payments. Proceeds payable under any policy shall, at Collateral Agent's option, be payable to Collateral Agent, for the ratable benefit of the Lenders, on account of the Obligations. Notwithstanding the foregoing, (a) so long as no Event of Default has occurred and is continuing, Borrower shall have the option of applying the proceeds of any casualty policy up to Two Hundred Fifty Thousand Dollars ($250,000.00) with respect to any loss, but not exceeding Three Hundred Fifty Thousand Dollars ($350,000.00), in the aggregate for all losses under all casualty policies in any one year, toward the replacement or repair of destroyed or damaged property; provided that any such replaced or repaired property (i) shall be of equal or like value as the replaced or repaired Collateral and (ii) shall be deemed Collateral in which Collateral Agent has been granted a first priority security interest subject only to Permitted Liens, and (b) after the occurrence and during the continuance of an Event of Default, all proceeds payable under such casualty policy shall, at the option of Collateral Agent, be payable to Collateral Agent, for the ratable benefit of the Lenders, on account of the Obligations then due. If Borrower or any of its Subsidiaries fails to obtain insurance as required under this Section 6.5 or to timely pay any amount or furnish any required proof of payment to third persons, Collateral Agent and/or any Lender may make, at Borrower's expense, all or part of such payment or obtain such insurance policies required in this Section 6.5, and take any action under the policies Collateral Agent or such Lender reasonably deems prudent.

6.6 Operating Accounts.

(a) Maintain all of Borrower's and its Subsidiaries' primary Collateral Accounts with Bank or its Affiliates in accounts which are subject to a Control Agreement in favor of Collateral Agent.

(b) Borrower shall provide Collateral Agent five (5) days' prior written notice before Borrower or any of its Subsidiaries establishes any Collateral Account at or with any Person other than Bank or its Affiliates. In addition, for each domestic Collateral Account that Borrower or any of its Subsidiaries, at any time maintains, Borrower or such Subsidiary shall cause the applicable bank or financial institution at or with which such domestic Collateral Account is maintained to execute and deliver a Control Agreement or other appropriate instrument with respect to such Collateral Account to perfect Collateral Agent's Lien in such Collateral Account in accordance with the terms hereunder prior to the establishment of such Collateral Account, which Control Agreement may not be terminated without prior written consent of Collateral Agent. The provisions of the previous sentence shall not apply to deposit accounts exclusively used for payroll, payroll taxes and other employee wage and benefit payments to or for the benefit of Borrower's, or any of its Subsidiaries', employees and identified to Collateral Agent by Borrower as such in the Perfection Certificates.

(c) Neither Borrower nor any of its Subsidiaries shall maintain any Collateral Accounts except Collateral Accounts maintained in accordance with Sections 6.6(a) and (b).

6.7 Protection of Intellectual Property Rights. Borrower and each of its Subsidiaries shall use commercially reasonable efforts to (a) protect, defend and maintain the validity and enforceability of its Intellectual Property that is material to Borrower's business; (b) promptly advise Collateral Agent and each Required Lender in writing of material infringement by a third party of its Intellectual Property; and (c) not allow any Intellectual Property material to Borrower's business to be abandoned, forfeited or dedicated to the public without Collateral Agent's prior written consent.

6.8 Litigation Cooperation. Commencing on the Effective Date and continuing through the termination of this Agreement, make available to Collateral Agent and the Lenders, without expense to Collateral Agent or the Lenders, Borrower and each of Borrower's officers, employees and agents and Borrower's Books, to the extent that Collateral Agent or any Lender may reasonably deem them necessary to prosecute or defend any third-party suit or proceeding instituted by or against Collateral Agent or any Lender with respect to any Collateral or relating to Borrower.

6.9 Notices of Litigation and Default. Borrower will give prompt written notice to Collateral Agent and the Required Lenders of any litigation or governmental proceedings pending or threatened (in writing) against Borrower or any of its Subsidiaries, which could reasonably be expected to result in damages or costs to Borrower or any of its Subsidiaries of Two Hundred Fifty Thousand Dollars ($250,000.00) or more or which could reasonably be expected to have a Material Adverse Change. Without limiting or contradicting any other more specific provision of this Agreement, promptly (and in any event within three (3) Business Days) upon Borrower becoming aware of the existence of any Event of Default or event which, with the giving of notice or passage of time, or both, would constitute an Event of Default, Borrower shall give written notice to Collateral Agent and the Lenders of such occurrence, which such notice shall include a reasonably detailed description of such Event of Default or event which, with the giving of notice or passage of time, or both, would constitute an Event of Default.

6.10 Phase 1 Trial Initiation. Within sixty (60) days of the Funding Date of the Term C Loan, if at all, Borrower will provide evidence to the Collateral Agent and each Required Lender, in form and content reasonably acceptable to Collateral Agent and the Required Lenders, of initiation of "iMod.Fc" Phase 1 clinical trial in the United States or European Union.

6.11 Landlord Waivers; Bailee Waivers. In the event that Borrower or any of its Subsidiaries which are parties to the Loan Documents, after the Effective Date, intends to add any new offices or business locations, including warehouses, or otherwise store any portion of the Collateral with, or deliver any portion of the Collateral to, a bailee, in each case pursuant to Section 7.2, then Borrower or such Subsidiary will, in the event that the new location is the chief executive office of the Borrower or such Subsidiary or the Collateral at any such new location is valued (on a book value basis) in excess of Two Hundred Fifty Thousand Dollars ($250,000.00) in the aggregate (other than other than pre-commercial drug substances and products and pre-filled syringes for clinical trials having an aggregate book value not in excess of Two Hundred Fifty Thousand Dollars ($250,000.00)), Borrower or such Subsidiary must cause such bailee or landlord, as applicable, to execute and deliver a bailee waiver or landlord waiver, as applicable, in form and substance reasonably satisfactory to Collateral Agent prior to the addition of any new offices or business locations, or any such storage with or delivery to any such bailee, as the case may be.

6.12 Creation/Acquisition of Subsidiaries. In the event Borrower, or any of its Subsidiaries creates or acquires any Subsidiary, Borrower shall provide prior written notice to Collateral Agent and each Required Lender of the creation or acquisition of such new Subsidiary and take all such action as may be reasonably required by Collateral Agent or any Required Lender to cause each any such Domestic Subsidiary to become a co-Borrower hereunder or to guarantee the Obligations of Borrower under the Loan Documents and, in each case, grant a continuing pledge and security interest in and to the assets of such Subsidiary (substantially as described on Exhibit A hereto); and Borrower (or its Subsidiary, as applicable) shall grant and pledge to Collateral Agent, for the ratable benefit of the Lenders, a perfected security interest in (a) the Shares of each such newly created Domestic Subsidiary and (b) sixty-five percent (65.00%) of the voting stock of any Foreign Subsidiary.

6.13 Further Assurances.

(a) Execute any further instruments and take further action as Collateral Agent or any Required Lender reasonably requests to perfect or continue Collateral Agent's Lien in the Collateral or to effect the purposes of this Agreement.

(b) Deliver to Collateral Agent and Lenders, within five (5) days after the same are sent or received, copies of all material correspondence, reports, documents and other filings with any Governmental Authority that could reasonably be expected to have a material adverse effect on any of the Governmental Approvals material to Borrower's business or otherwise could reasonably be expected to have a Material Adverse Change.

* Confidential information, indicated [***], has been omitted from this filing and filed separately with the Securities and Exchange Commission.

7. NEGATIVE COVENANTS

Borrower shall not, and shall not permit any of its Subsidiaries to, do any of the following without the prior written consent of the Required Lenders:

7.1 Dispositions. Convey, sell, lease, transfer, assign, or otherwise dispose of (collectively, " **Transfer**"), or permit any of its Subsidiaries to Transfer, all or any part of its business or property, except for Transfers (a) of Inventory in the ordinary course of business; (b) of worn out, surplus or obsolete Equipment; (c) in connection with Permitted Liens, Permitted Investments and Permitted Licenses; (d) consisting of the use or transfer of money or Cash Equivalents in the ordinary course of Borrower's business and a manner that is not prohibited by the terms of this Agreement or the other Loan Documents; (e) of non-exclusive licenses for the use of the Intellectual Property of Borrower its Subsidiaries in the ordinary course of business and that could not result in a legal transfer of the licensed property but that may be exclusive as to territory only as to discrete geographical areas outside of the United States; and (f) other dispositions not exceeding One Hundred Thousand Dollars ($100,000.00) in any fiscal year.

7.2 Changes in Business; Change in Control; Jurisdiction of Formation. Engage in any material line of business other than those lines of business conducted by Borrower and its Subsidiaries on the date hereof and any businesses reasonably related, complementary or incidental thereto or reasonable extensions thereof; or permit or suffer any Change in Control. Borrower will not, without prior written notice to Bank: (i) change its jurisdiction of organization, (ii) change its organizational structure or type, (iii) change its legal name, (iv) change any organizational number (if any) assigned by its jurisdiction of organization, or add any new offices or business locations, including warehouses (unless such new offices or business locations contain less than Two Hundred Fifty Thousand Dollars ($250,000.00) in book value in Borrower's assets or property (other than pre-commercial drug substances and products and pre-filled syringes for clinical trials having a book value not to exceed Two Hundred Fifty Thousand Dollars ($250,000.00)) or deliver any portion of the Collateral valued (on a book value basis), individually or in the aggregate, in excess of Two Hundred Fifty Thousand Dollars ($250,000.00) (other than pre-commercial drug substances and products and pre-filled syringes for clinical trials having a book value not to exceed Two Hundred Fifty Thousand Dollars ($250,000.00)) to a bailee at a location other than to a bailee and at a location already disclosed in the Perfection Certificate. If Borrower intends to deliver any portion of the Collateral valued (on a book value basis), individually or in the aggregate, in excess of Two Hundred Fifty Thousand Dollars ($250,000.00) (other than pre-commercial drug substances and products and pre-filled syringes for clinical trials having a book value not to exceed Two Hundred Fifty Thousand Dollars ($250,000.00)) to a bailee, and Bank and such bailee are not already parties to a bailee agreement governing both the Collateral and the location to which Borrower intends to deliver the Collateral, then Borrower will cause such bailee shall execute and deliver a bailee agreement in form and substance satisfactory to Bank in its reasonable discretion.

7.3 Mergers or Acquisitions. Merge or consolidate, or permit any of its Subsidiaries to merge or consolidate, with any other Person, or acquire, or permit any of its Subsidiaries to acquire, all or substantially all of the capital stock, shares or property of another Person. A Subsidiary may merge or consolidate into another Subsidiary (provided that if the merger involves a Subsidiary which is a "co-Borrower" hereunder, such surviving Subsidiary is a "co-Borrower" hereunder or has provided a secured Guaranty of Borrower's Obligations hereunder) or with (or into) Borrower provided Borrower is the surviving legal entity, and as long as no Event of Default is occurring prior thereto or arises as a result therefrom.

7.4 Indebtedness. Create, incur, assume, or be liable for any Indebtedness, or permit any Subsidiary to do so, other than Permitted Indebtedness.

7.5 Encumbrance. Create, incur, allow, or suffer any Lien on any of its property, or assign or convey any right to receive income, including the sale of any Accounts, or permit any of its Subsidiaries to do so, except for Permitted Liens, or permit any Collateral not to be subject to the first priority security interest granted herein (except for Permitted Liens that are permitted by the terms of this Agreement to have priority over Collateral Agent's Lien), or enter into any agreement, document, instrument or other arrangement (except with or in favor of Collateral Agent, for the ratable benefit of the Lenders) with any Person which directly or indirectly prohibits or has the effect of prohibiting Borrower, or any of its Subsidiaries, from assigning, mortgaging, pledging, granting a security interest in or upon, or encumbering any of Borrower's or such Subsidiary's Intellectual Property, except as is otherwise permitted in Section 7.1 hereof and the definition of "**Permitted Liens**" herein.

7.6 Maintenance of Collateral Accounts. Maintain any Collateral Account except pursuant to the terms of Section 6.6 hereof.

7.7 Distributions; Investments. (a) Pay any dividends (other than dividends payable solely in capital stock) or make any distribution or payment in respect of or redeem, retire or purchase any capital stock (other than (i) repurchases pursuant to the terms of employee stock purchase plans, employee restricted stock agreements, stockholder rights plans, director or consultant stock option plans, or similar plans, provided such repurchases do not exceed Two Hundred Fifty Thousand Dollars ($250,000.00) in the aggregate per fiscal year and , (ii) conversion of any of its convertible securities into other securities) or (b) directly or indirectly make any Investment other than Permitted Investments, or permit any of its Subsidiaries to do so.

7.8 Transactions with Affiliates. Directly or indirectly enter into or permit to exist any material transaction with any Affiliate of Borrower or any of its Subsidiaries, except for (a) transactions that are in the ordinary course of Borrower's or such Subsidiary's business, upon fair and reasonable terms that are no less favorable to Borrower or such Subsidiary than would be obtained in an arm's length transaction with a non-affiliated Person, (b) Subordinated Debt or equity investments by Borrower's investors in Borrower or its Subsidiaries, (c) customary director, officer and employee compensation (including bonuses) and other benefits (including retirement, health, stock option and other benefit plans and indemnification arrangements approved by the relevant board of directors, board of managers or equivalent corporate body, (d) transactions permitted pursuant to Sections 7.1, 7.2, 7.4 and 7.7; (e) licensing arrangements between Borrower and Pangu pursuant to that certain License Agreement, dated May 16, 2008 between Borrower and Pangu, as amended, restated, supplemented, replaced or modified from time to time; and (f) transactions pursuant to that certain Research Funding and Option Agreement between and among the Borrower, The Scripps Research Institute and aaRS, LLC.

7.9 Subordinated Debt. (a) Make or permit any payment on any Subordinated Debt, except under the terms of the subordination, intercreditor, or other similar agreement to which such Subordinated Debt is subject, or (b) amend any provision in any document relating to the Subordinated Debt which would increase the amount thereof or adversely affect the subordination thereof to Obligations owed to the Lenders.

7.10 Compliance. Become an "investment company" or a company controlled by an "investment company", under the Investment Company Act of 1940, as amended, or undertake as one of its important activities extending credit to purchase or carry margin stock (as defined in Regulation U of the Board of Governors of the Federal Reserve System), or use the proceeds of any Credit Extension for that purpose; fail to meet the minimum funding requirements of ERISA, permit a Reportable Event or Prohibited Transaction, as defined in ERISA, to occur; fail to comply with applicable provisions of the Federal Fair Labor Standards Act or violate any other law or regulation, in each case, if the failure to comply or violation could reasonably be expected to have a Material Adverse Change, or permit any of its Subsidiaries to do so; withdraw or permit any Subsidiary to withdraw from participation in, permit partial or complete termination of, or permit the occurrence of any other event with respect to, any present pension, profit sharing and deferred compensation plan which could reasonably be expected to result in any liability of Borrower or any of its Subsidiaries, including any liability to the Pension Benefit Guaranty Corporation or its successors or any other Governmental Authority.

7.11 Compliance with Anti-Terrorism Laws. Collateral Agent hereby notifies Borrower and each of its Subsidiaries that pursuant to the requirements of Anti-Terrorism Laws, and Collateral Agent's policies and practices, Collateral Agent is required to obtain, verify and record certain information and documentation that identifies Borrower and each of its Subsidiaries and their principals, which information includes the name and address of Borrower and each of its Subsidiaries and their principals and such other information that will allow Collateral Agent to identify such party in accordance with Anti-Terrorism Laws. Neither Borrower nor any of its Subsidiaries shall, nor shall Borrower or any of its Subsidiaries knowingly permit any Affiliate to, directly or indirectly, knowingly enter into any documents, instruments, agreements or contracts with any Person listed on the OFAC Lists. Borrower and each of its Subsidiaries shall immediately notify Collateral Agent if Borrower or such Subsidiary has knowledge that Borrower, or any Subsidiary or Affiliate of Borrower, is listed on the OFAC Lists or (a) is convicted on, (b) pleads *nolo contendere* to, (c) is indicted on, or (d) is arraigned and held over on charges involving money laundering or predicate crimes to money laundering. Neither Borrower nor any of its Subsidiaries shall, nor shall Borrower or any of its Subsidiaries, knowingly permit any Affiliate to, directly or indirectly, (i) conduct any business or engage in any transaction or dealing with any Blocked Person, including, without limitation, the making or receiving of any contribution of funds, goods or services to or for the benefit of any

Blocked Person, (ii) deal in, or otherwise engage in any transaction relating to, any property or interests in property blocked pursuant to Executive Order No. 13224 or any similar executive order or other Anti-Terrorism Law, or (iii) engage in or conspire to engage in any transaction that evades or avoids, or has the purpose of evading or avoiding, or attempts to violate, any of the prohibitions set forth in Executive Order No. 13224 or other Anti-Terrorism Law.

7.12 Assets in Pangu. Transfer to, or permit Pangu to hold or maintain, at any time assets (excluding Pangu's interest in Intellectual Property jointly developed with Borrower from time to time) of an aggregate value in excess of Two Hundred Fifty Thousand Dollars ($250,000.00).

8. EVENTS OF DEFAULT

Any one of the following shall constitute an event of default (an "**Event of Default**") under this Agreement:

8.1 Payment Default. Borrower fails to (a) make any payment of principal or interest on any Credit Extension on its due date, or (b) pay any other Obligations within three (3) Business Days after such Obligations are due and payable (which three (3) Business Day grace period shall not apply to payments due on the Maturity Date or the date of acceleration pursuant to Section 9.1 (a) hereof). During the cure period, the failure to cure the payment default is not an Event of Default (but no Credit Extension will be made during the cure period);

8.2 Covenant Default.

(a) Borrower or any of its Subsidiaries fails or neglects to perform any obligation in Sections 6.2 (Financial Statements, Reports, Certificates), 6.4 (Taxes), 6.5 (Insurance), 6.6 (Operating Accounts), 6.7 (Protection of Intellectual Property Rights), 6.9 (Notice of Litigation and Default), 6.10 (Phase 1 Trial Initiation), 6.11 (Landlord Waivers; Bailee Waivers), 6.12 (Creation/Acquisition of Subsidiaries) or 6.13 (Further Assurances) or Borrower violates any covenant in Section 7; or

(b) Borrower, or any of its Subsidiaries, fails or neglects to perform, keep, or observe any other term, provision, condition, covenant or agreement contained in this Agreement or any Loan Documents, and as to any default (other than those specified in this Section 8) under such other term, provision, condition, covenant or agreement that can be cured, has failed to cure the default within ten (10) days after the occurrence thereof; provided, however, that if the default cannot by its nature be cured within the ten (10) day period or cannot after diligent attempts by Borrower be cured within such ten (10) day period, and such default is likely to be cured within a reasonable time, then Borrower shall have an additional period (which shall not in any case exceed thirty (30) days) to attempt to cure such default, and within such reasonable time period the failure to cure the default shall not be deemed an Event of Default (but no Credit Extensions shall be made during such cure period). Grace periods provided under this Section shall not apply, among other things, to financial covenants or any other covenants set forth in subsection (a) above;

8.3 Material Adverse Change. A Material Adverse Change occurs;

8.4 Attachment; Levy; Restraint on Business.

(a) (i) The service of process seeking to attach, by trustee or similar process, any funds of Borrower or any of its Subsidiaries or of any entity under control of Borrower or its Subsidiaries on deposit with any Lender or any Lender's Affiliate or any bank or other institution at which Borrower or any of its Subsidiaries maintains a Collateral Account, or (ii) a notice of lien, levy, or assessment is filed against Borrower or any of its Subsidiaries or their respective assets by any government agency, and the same under subclauses (i) and (ii) hereof are not, within ten (10) days after the occurrence thereof, discharged or stayed (whether through the posting of a bond or otherwise); provided, however, no Credit Extensions shall be made during any ten (10) day cure period; and

(b) (i) any material portion of Borrower's or any of its Subsidiaries' assets is attached, seized, levied on, or comes into possession of a trustee or receiver, or (ii) any court order enjoins, restrains, or prevents Borrower or any of its Subsidiaries from conducting all or any material part of its business;

8.5 Insolvency. (a) Borrower is, and Borrower and each of its Subsidiaries, taken as a whole on a consolidated basis, are or become Insolvent; (b) Borrower or any of its Subsidiaries begins an Insolvency Proceeding; or (c) an Insolvency Proceeding is begun against Borrower or any of its Subsidiaries and not dismissed or stayed within forty-five (45) days (but no Credit Extensions shall be made while Borrower or any Subsidiary is Insolvent and/or until any Insolvency Proceeding is dismissed);

8.6 Other Agreements. There is a default in any agreement to which Borrower or any of its Subsidiaries is a party with a third party or parties resulting in a right by such third party or parties, whether or not exercised, to accelerate the maturity of any Indebtedness in an amount in excess of Two Hundred Fifty Thousand Dollars ($250,000.00) or that could reasonably be expected to have a Material Adverse Change;

8.7 Judgments. One or more judgments, orders, or decrees for the payment of money in an amount, individually or in the aggregate, of at least Two Hundred Fifty Thousand Dollars ($250,000.00) (not covered by independent third-party insurance as to which liability has been accepted by such insurance carrier) shall be rendered against Borrower or any of its Subsidiaries and shall remain unsatisfied, unvacated, or unstayed for a period of ten (10) days after the entry thereof (provided that no Credit Extensions will be made prior to the satisfaction, vacation, or stay of such judgment, order or decree);

8.8 Misrepresentations. Borrower or any of its Subsidiaries or any Person acting for Borrower or any of its Subsidiaries makes any representation, warranty, or other statement now or later in this Agreement, any Loan Document or in any writing delivered to Collateral Agent and/or Lenders or to induce Collateral Agent and/or the Lenders to enter this Agreement or any Loan Document, and such representation, warranty, or other statement is incorrect in any material respect when made;

8.9 Subordinated Debt. A default or breach occurs under any agreement between Borrower or any of its Subsidiaries and any creditor of Borrower or any of its Subsidiaries that signed a subordination, intercreditor, or other similar agreement with Collateral Agent or the Lenders, or any creditor that has signed such subordination, intercreditor or similar agreement with Collateral Agent or the Lenders breaches any terms of such agreement;

8.10 Guaranty. (a) Any Guaranty terminates or ceases for any reason to be in full force and effect; (b) any Guarantor does not perform any obligation or covenant under any Guaranty and such breach is not cured within any applicable cure period there within; (c) any circumstance described in Sections 8.3, 8.4, 8.5, 8.7, or 8.8 occurs with respect to any Guarantor, or (d) the liquidation, winding up, or termination of existence of any Guarantor;

8.11 Governmental Approvals; FDA Action. (a) Any Governmental Approval shall have been revoked, rescinded, suspended, modified in an adverse manner, or not renewed in the ordinary course for a full term *and* such revocation, rescission, suspension, modification or non-renewal has resulted in or could reasonably be expected to result in a Material Adverse Change; or (b) (i) the FDA, DOJ or other Governmental Authority initiates a Regulatory Action or any other enforcement action against Borrower or any of its Subsidiaries or any supplier of Borrower or any of its Subsidiaries that causes Borrower or any of its Subsidiaries to recall, withdraw, remove or discontinue manufacturing, distributing, and/or marketing any of its products, even if such action is based on previously disclosed conduct which recall, withdraw, removal or discontinuance could reasonably be expected to result in liability and expense of Two Hundred Fifty Thousand Dollars ($250,000.00) or more; (ii) the FDA issues a warning letter to Borrower or any of its Subsidiaries with respect to any of its activities or products which could reasonably be expected to result in a Material Adverse Change; (iii) Borrower or any of its Subsidiaries conducts a mandatory or voluntary recall which could reasonably be expected to result in liability and expense to Borrower or any of its Subsidiaries of Two Hundred Fifty Thousand Dollars ($250,000.00) or more; (iv) Borrower or any of its Subsidiaries enters into a settlement agreement with the FDA, DOJ or other Governmental Authority that results in aggregate liability as to any single or related series of transactions, incidents or conditions, of Two Hundred Fifty Thousand Dollars ($250,000.00) or more, or that could reasonably be expected to result in a Material Adverse Change, even if such settlement agreement is based on previously disclosed conduct; or (v) the FDA revokes any authorization or permission granted under any Registration, or Borrower or any of its Subsidiaries withdraws any Registration, that could reasonably be expected to result in a Material Adverse Change.

8.12 Lien Priority. Any Lien created hereunder or by any other Loan Document shall at any time fail to constitute a valid and perfected Lien on any of the Collateral purported to be secured thereby, subject to no prior

or equal Lien, other than Permitted Liens which are permitted to have priority in accordance with the terms of this Agreement.

9. RIGHTS AND REMEDIES

9.1 Rights and Remedies.

(a) Upon the occurrence and during the continuance of an Event of Default, Collateral Agent may, and at the written direction of Required Lenders shall, without notice or demand, do any or all of the following: (i) deliver notice of the Event of Default to Borrower, (ii) by notice to Borrower declare all Obligations immediately due and payable (but if an Event of Default described in Section 8.5 occurs all Obligations shall be immediately due and payable without any action by Collateral Agent or the Lenders) or (iii) by notice to Borrower suspend or terminate the obligations, if any, of the Lenders to advance money or extend credit for Borrower's benefit under this Agreement or under any other agreement between Borrower and Collateral Agent and/or the Lenders (but if an Event of Default described in Section 8.5 occurs all obligations, if any, of the Lenders to advance money or extend credit for Borrower's benefit under this Agreement or under any other agreement between Borrower and Collateral Agent and/or the Lenders shall be immediately terminated without any action by Collateral Agent or the Lenders).

(b) Without limiting the rights of Collateral Agent and the Lenders set forth in Section 9.1(a) above, upon the occurrence and during the continuance of an Event of Default, Collateral Agent shall have the right and at the written direction of the Required Lenders shall, without notice or demand, to do any or all of the following:

(i) foreclose upon and/or sell or otherwise liquidate, the Collateral;

(ii) apply to the Obligations any (a) balances and deposits of Borrower that Collateral Agent or any Lender holds or controls, or (b) any amount held or controlled by Collateral Agent or any Lender owing to or for the credit or the account of Borrower; and/or

(iii) commence and prosecute an Insolvency Proceeding or consent to Borrower commencing any Insolvency Proceeding.

(c) Without limiting the rights of Collateral Agent and the Lenders set forth in Sections 9.1(a) and (b) above, upon the occurrence and during the continuance of an Event of Default, Collateral Agent shall have the right and at the written direction of the Required Lenders shall, without notice or demand, to do any or all of the following:

(i) settle or adjust disputes and claims directly with Account Debtors for amounts on terms and in any order that Collateral Agent considers advisable, notify any Person owing Borrower money of Collateral Agent's security interest in such funds, and verify the amount of such account;

(ii) make any payments and do any acts it considers necessary or reasonable to protect the Collateral and/or its security interest in the Collateral. Borrower shall assemble the Collateral if Collateral Agent requests and make it available in a location as Collateral Agent reasonably designates. Collateral Agent may enter premises where the Collateral is located, take and maintain possession of any part of the Collateral, and pay, purchase, contest, or compromise any Lien which appears to be prior or superior to its security interest and pay all expenses incurred. Borrower grants Collateral Agent a license to enter and occupy any of its premises, without charge, to exercise any of Collateral Agent's rights or remedies;

(iii) ship, reclaim, recover, store, finish, maintain, repair, prepare for sale, and/or advertise for sale, the Collateral. Collateral Agent is hereby granted a non-exclusive, royalty-free license or other right to use, without charge, Borrower's and each of its Subsidiaries' labels, patents, copyrights, mask works, rights of use of any name, trade secrets, trade names, trademarks, service marks, and advertising matter, or any similar property as it pertains to the Collateral, in completing production of, advertising for sale, and selling any Collateral and, in connection with Collateral Agent's exercise of its rights under this Section 9.1, Borrower's and each of its

Subsidiaries' rights under all licenses and all franchise agreements inure to Collateral Agent, for the benefit of the Lenders;

(iv) place a "hold" on any account maintained with Collateral Agent or the Lenders and/or deliver a notice of exclusive control, any entitlement order, or other directions or instructions pursuant to any Control Agreement or similar agreements providing control of any Collateral;

(v) demand and receive possession of Borrower's Books;

(vi) appoint a receiver to seize, manage and realize any of the Collateral, and such receiver shall have any right and authority as any competent court will grant or authorize in accordance with any applicable law, including any power or authority to manage the business of Borrower or any of its Subsidiaries;

(vii) subject to clauses 9.1(a) and (b), exercise all rights and remedies available to Collateral Agent and each Lender under the Loan Documents or at law or equity, including all remedies provided under the Code (including disposal of the Collateral pursuant to the terms thereof);

(viii) for any Letters of Credit, demand that Borrower (i) deposit cash with Bank in an amount equal to (x) if such Letters of Credit are denominated in Dollars, then one hundred five percent (105%); and (y) if such Letters of Credit are denominated in a Foreign Currency, then one hundred ten percent (110%), of the Dollar Equivalent of the aggregate face amount of all Letters of Credit remaining undrawn (plus all interest, fees, and costs due or to become due in connection therewith (as estimated by Bank in its good faith business judgment)), to secure all of the Obligations relating to such Letters of Credit, as collateral security for the repayment of any future drawings under such Letters of Credit, and Borrower shall forthwith deposit and pay such amounts, and (ii) pay in advance all letter of credit fees scheduled to be paid or payable over the remaining term of any Letters of Credit; and

(ix) terminate any FX Contracts.

Notwithstanding any provision of this Section 9.1 to the contrary, upon the occurrence of any Event of Default, Collateral Agent shall have the right to exercise any and all remedies referenced in this Section 9.1 without the written consent of Required Lenders following the occurrence of an Exigent Circumstance.

9.2 Power of Attorney. Borrower hereby irrevocably appoints Collateral Agent as its lawful attorney-in-fact, exercisable solely upon the occurrence and during the continuance of an Event of Default, to: (a) endorse Borrower's or any of its Subsidiaries' name on any checks or other forms of payment or security; (b) sign Borrower's or any of its Subsidiaries' name on any invoice or bill of lading for any Account or drafts against Account Debtors; (c) settle and adjust disputes and claims about the Accounts directly with Account Debtors, for amounts and on terms Collateral Agent determines reasonable; (d) make, settle, and adjust all claims under Borrower's insurance policies; (e) pay, contest or settle any Lien, charge, encumbrance, security interest, and adverse claim in or to the Collateral, or any judgment based thereon, or otherwise take any action to terminate or discharge the same; and (f) transfer the Collateral into the name of Collateral Agent or a third party as the Code or any applicable law permits. Borrower hereby appoints Collateral Agent as its lawful attorney-in-fact to sign Borrower's or any of its Subsidiaries' name on any documents necessary to perfect or continue the perfection of Collateral Agent's security interest in the Collateral regardless of whether an Event of Default has occurred until all Obligations (other than inchoate indemnity or reimbursement obligations or other obligations which, by their terms, survive termination of this Agreement) have been satisfied in full and Collateral Agent and the Lenders are under no further obligation to make Credit Extensions hereunder. Collateral Agent's foregoing appointment as Borrower's or any of its Subsidiaries' attorney in fact, and all of Collateral Agent's rights and powers, coupled with an interest, are irrevocable until all Obligations (other than inchoate indemnity or reimbursement obligations or other obligations which, by their terms, survive termination of this Agreement) have been fully repaid and performed and Collateral Agent's and the Lenders' obligation to provide Credit Extensions terminates.

9.3 Protective Payments. If Borrower or any of its Subsidiaries fail to timely obtain the insurance called for by Section 6.5 or fails to timely pay any premium thereon or fails to pay any other amount which Borrower or any of its Subsidiaries is obligated to pay under this Agreement or any other Loan Document, Collateral Agent may obtain such insurance or make such payment, and all amounts so paid by Collateral Agent are Lenders'

Expenses and immediately due and payable, bearing interest at the Default Rate, and secured by the Collateral. Collateral Agent will make reasonable efforts to provide Borrower with notice of Collateral Agent obtaining such insurance or making such payment at the time it is obtained or paid or within a reasonable time thereafter. No such payments by Collateral Agent are deemed an agreement to make similar payments in the future or Collateral Agent's waiver of any Event of Default.

9.4 Application of Payments and Proceeds. Notwithstanding anything to the contrary contained in this Agreement, upon the occurrence and during the continuance of an Event of Default, (a) Borrower irrevocably waives the right to direct the application of any and all payments at any time or times thereafter received by Collateral Agent from or on behalf of Borrower or any of its Subsidiaries of all or any part of the Obligations, and, as between Borrower on the one hand and Collateral Agent and Lenders on the other, Collateral Agent shall have the continuing and exclusive right to apply and to reapply any and all payments received against the Obligations in such manner as Collateral Agent may deem advisable notwithstanding any previous application by Collateral Agent, and (b) the proceeds of any sale of, or other realization upon all or any part of the Collateral shall be applied: first, to the Lenders' Expenses; second, to accrued and unpaid interest on the Obligations (including any interest which, but for the provisions of the United States Bankruptcy Code, would have accrued on such amounts); third, to the principal amount of the Obligations outstanding; and fourth, to any other indebtedness or obligations of Borrower owing to Collateral Agent or any Lender under the Loan Documents. Any balance remaining shall be delivered to Borrower or to whoever may be lawfully entitled to receive such balance or as a court of competent jurisdiction may direct. In carrying out the foregoing, (x) amounts received shall be applied in the numerical order provided until exhausted prior to the application to the next succeeding category, and (y) each of the Persons entitled to receive a payment in any particular category shall receive an amount equal to its pro rata share of amounts available to be applied pursuant thereto for such category. Any reference in this Agreement to an allocation between or sharing by the Lenders of any right, interest or obligation "ratably," "proportionally" or in similar terms shall refer to Pro Rata Share unless expressly provided otherwise. Collateral Agent, or if applicable, each Lender, shall promptly remit to the other Lenders such sums as may be necessary to ensure the ratable repayment of each Lender's portion of any Term Loan and the ratable distribution of interest, fees and reimbursements paid or made by Borrower. Notwithstanding the foregoing, a Lender receiving a scheduled payment shall not be responsible for determining whether the other Lenders also received their scheduled payment on such date; provided, however, if it is later determined that a Lender received more than its ratable share of scheduled payments made on any date or dates, then such Lender shall remit to Collateral Agent or other Lenders such sums as may be necessary to ensure the ratable payment of such scheduled payments, as instructed by Collateral Agent. If any payment or distribution of any kind or character, whether in cash, properties or securities, shall be received by a Lender in excess of its ratable share, then the portion of such payment or distribution in excess of such Lender's ratable share shall be received by such Lender in trust for and shall be promptly paid over to the other Lender for application to the payments of amounts due on the other Lenders' claims. To the extent any payment for the account of Borrower is required to be returned as a voidable transfer or otherwise, the Lenders shall contribute to one another as is necessary to ensure that such return of payment is on a pro rata basis. If any Lender shall obtain possession of any Collateral, it shall hold such Collateral for itself and as agent and bailee for Collateral Agent and other Lenders for purposes of perfecting Collateral Agent's security interest therein.

9.5 Liability for Collateral. So long as Collateral Agent and the Lenders comply with reasonable banking practices regarding the safekeeping of the Collateral in the possession or under the control of Collateral Agent and the Lenders, Collateral Agent and the Lenders shall not be liable or responsible for: (a) the safekeeping of the Collateral; (b) any loss or damage to the Collateral; (c) any diminution in the value of the Collateral; or (d) any act or default of any carrier, warehouseman, bailee, or other Person. So long as Collateral Agent and the Lenders comply with reasonable banking practices, Borrower bears all risk of loss, damage or destruction of the Collateral.

9.6 No Waiver; Remedies Cumulative. Failure by Collateral Agent or any Lender, at any time or times, to require strict performance by Borrower of any provision of this Agreement or any other Loan Document shall not waive, affect, or diminish any right of Collateral Agent or any Lender thereafter to demand strict performance and compliance herewith or therewith. No waiver hereunder shall be effective unless signed by Collateral Agent and the Required Lenders and then is only effective for the specific instance and purpose for which it is given. The rights and remedies of Collateral Agent and the Lenders under this Agreement and the other Loan Documents are cumulative. Collateral Agent and the Lenders have all rights and remedies provided under the Code, any applicable law, by law, or in equity. The exercise by Collateral Agent or any Lender of one right or remedy is

not an election, and Collateral Agent's or any Lender's waiver of any Event of Default is not a continuing waiver. Collateral Agent's or any Lender's delay in exercising any remedy is not a waiver, election, or acquiescence.

9.7 Demand Waiver. Borrower waives, to the fullest extent permitted by law, demand, notice of default or dishonor, notice of payment and nonpayment, notice of any default, nonpayment at maturity, release, compromise, settlement, extension, or renewal of accounts, documents, instruments, chattel paper, and guarantees held by Collateral Agent or any Lender on which Borrower or any Subsidiary is liable.

10. NOTICES

All notices, consents, requests, approvals, demands, or other communication (collectively, "**Communication**") by any party to this Agreement or any other Loan Document must be in writing and shall be deemed to have been validly served, given, or delivered: (a) upon the earlier of actual receipt and three (3) Business Days after deposit in the U.S. mail, first class, registered or certified mail return receipt requested, with proper postage prepaid; (b) upon transmission, when sent by electronic mail or facsimile transmission; (c) one (1) Business Day after deposit with a reputable overnight courier with all charges prepaid; or (d) when delivered, if hand-delivered by messenger, all of which shall be addressed to the party to be notified and sent to the address, facsimile number, or email address indicated below. Any of Collateral Agent, Lender or Borrower may change its mailing address or electronic mail or facsimile number by giving the other party written notice thereof in accordance with the terms of this Section 10.

If to Borrower:	ATYR PHARMA, INC. 3545 John Hopkins Court, Suite 250 San Diego, CA 92121 Attn: John Blake Fax: (858) 875-1110 Email:
with a copy (which shall not constitute notice) to:	Goodwin Proctor LLP 100 Northern Avenue Boston, MA 02210 Attn: Mark Smith Fax: (617) 801-8835 Email:
If to Collateral Agent:	SILICON VALLEY BANK 4370 La Jolla Village Drive, Suite 1050 San Diego, CA 92122 Attn: Anthony Flores –Director Fax: (858) 622-1424 Email:
with a copy (which shall not constitute notice) to:	DLA Piper LLP (US) 4365 Executive Drive, Suite 1100 San Diego, California 92121-2133 Attn: Troy Zander Fax: (858) 638-5086 Email:
with a copy to	SOLAR CAPITAL LTD. 500 Park Avenue, 3rd Floor New York, New York 10022 Attn: Neil Bonanno, Managing Director Fax: (212) 993-1698 Email:

* Confidential information, indicated [***], has been omitted from this filing and filed separately with the Securities and Exchange Commission.

with a copy (which shall not constitute notice) to:	LATHAM & WATKINS LLP 505 Montgomery Street, Suite 2000 San Francisco, CA 94111 Attention: Haim Zaltzman Facsimile: (415) 395-8095 Email:

11. CHOICE OF LAW, VENUE AND JURY TRIAL WAIVER, AND JUDICIAL REFERENCE

New York law governs the Loan Documents without regard to principles of conflicts of law. Borrower, Lenders and Collateral Agent each submit to the exclusive jurisdiction of the State and Federal courts in the City of New York, Borough of Manhattan. NOTWITHSTANDING THE FOREGOING, COLLATERAL AGENT AND THE LENDERS SHALL HAVE THE RIGHT TO BRING ANY ACTION OR PROCEEDING AGAINST BORROWER OR ITS PROPERTY IN THE COURTS OF ANY OTHER JURISDICTION WHICH COLLATERAL AGENT AND THE LENDERS (IN ACCORDANCE WITH THE PROVISIONS OF SECTION 9.1) DEEM NECESSARY OR APPROPRIATE TO REALIZE ON THE COLLATERAL OR TO OTHERWISE ENFO RCE COLLATERAL AGENT'S AND THE LENDERS' RIGHTS AGAINST BORROWER OR ITS PROPERTY. Borrower expressly submits and consents in advance to such jurisdiction in any action or suit commenced in any such court, and Borrower hereby waives any objection that it may have based upon lack of personal jurisdiction, improper venue, or forum non conveniens and hereby consents to the granting of such legal or equitable relief as is deemed appropriate by such court. Borrower hereby waives personal service of the summons, complaints, and other process issued in such action or suit and agrees that service of such summons, complaints, and other process may be made by registered or certified mail addressed to Borrower at the address set forth in, or subsequently provided by Borrower in accordance with, Section 10 of this Agreement and that service so made shall be deemed completed upon the earlier to occur of Borrower's actual receipt thereof or three (3) days after deposit in the U.S. mails, first class, registered or certified mail return receipt requested, proper postage prepaid.

TO THE FULLEST EXTENT PERMITTED BY APPLICABLE LAW, BORROWER, COLLATERAL AGENT, AND THE LENDERS EACH WAIVE THEIR RIGHT TO A JURY TRIAL OF ANY CLAIM OR CAUSE OF ACTION ARISING OUT OF OR BASED UPON THIS AGREEMENT, THE LOAN DOCUMENTS OR ANY CONTEMPLATED TRANSACTION, INCLUDING CONTRACT, TORT, BREACH OF DUTY AND ALL OTHER CLAIMS. THIS WAIVER IS A MATERIAL INDUCEMENT FOR EACH PARTY TO ENTER INTO THIS AGREEMENT. EACH PARTY HAS REVIEWED THIS WAIVER WITH ITS COUNSEL.

12. GENERAL PROVISIONS

12.1 Successors and Assigns. This Agreement binds and is for the benefit of the successors and permitted assigns of each party. Borrower may not transfer, pledge or assign this Agreement or any rights or obligations under it without Collateral Agent's and each Lender's prior written consent (which may be granted or withheld in Collateral Agent's and each Lender's discretion, subject to Section 12.6). The Lenders have the right, without the consent of or notice to Borrower, to sell, transfer, assign, pledge, negotiate, or grant participation in (any such sale, transfer, assignment, negotiation, or grant of a participation, a **"Lender Transfer")** all or any part of, or any interest in, the Lenders' obligations, rights, and benefits under this Agreement and the other Loan Documents; *provided*, *however*, that any such Lender Transfer (other than a transfer, pledge, sale or assignment to an Eligible Assignee) of its obligations, rights, and benefits under this Agreement and the other Loan Documents shall require the prior written consent of the Required Lenders (such approved assignee, an "**Approved Lender**"). Borrower and Collateral Agent shall be entitled to continue to deal solely and directly with such Lender in connection with the interests so assigned until Collateral Agent shall have received and accepted an effective assignment agreement in form satisfactory to Collateral Agent executed, delivered and fully completed by the applicable parties thereto, and shall have received such other information regarding such Eligible Assignee or Approved Lender as Collateral Agent reasonably shall require. Notwithstanding anything to the contrary contained herein, so long as no Event of Default has occurred and is continuing, no Lender Transfer (other than a Lender Transfer (i) in respect of the Warrants or (ii) in connection with (x) assignments by a Lender due to a forced divestiture at the request of any regulatory agency; or (y) upon the occurrence of a default, event of default or similar occurrence with respect to a Lender's own financing or securitization transactions) shall be permitted, without Borrower's consent, to any Person which is an Affiliate or Subsidiary of Borrower, a direct competitor of Borrower or a vulture hedge fund, each as determined by Collateral Agent.

* Confidential information, indicated [***], has been omitted from this filing and filed separately with the Securities and Exchange Commission.

12.2 Indemnification. Borrower agrees to indemnify, defend and hold Collateral Agent and the Lenders and their respective directors, officers, employees, agents, attorneys, or any other Person affiliated with or representing Collateral Agent or the Lenders (each, an "**Indemnified Person**") harmless against: (a) all obligations, demands, claims, and liabilities (collectively, "**Claims**") asserted by any other party in connection with; related to; following; or arising from, out of or under, the transactions contemplated by the Loan Documents; and (b) all documented losses or Lenders' Expenses incurred, or paid by Indemnified Person in connection with; related to; following; or arising from, out of or under, the transactions contemplated by the Loan Documents between Collateral Agent, and/or the Lenders and Borrower (including reasonable attorneys' fees and expenses), except for Claims and/or losses caused by any Indemnified Person's gross negligence or willful misconduct. Borrower hereby further indemnifies, defends and holds each Indemnified Person harmless from and against any and all liabilities, obligations, losses, damages, penalties, actions, judgments, suits, claims, costs, expenses and disbursements of any kind or nature whatsoever (including the fees and disbursements of counsel for such Indemnified Person) in connection with any investigative, response, remedial, administrative or judicial matter or proceeding, whether or not such Indemnified Person shall be designated a party thereto and including any such proceeding initiated by or on behalf of Borrower, and the reasonable expenses of investigation by engineers, environmental consultants and similar technical personnel and any commission, fee or compensation claimed by any broker (other than any broker retained by Collateral Agent or Lenders) asserting any right to payment for the transactions contemplated hereby which may be imposed on, incurred by or asserted against such Indemnified Person as a result of or in connection with the transactions contemplated hereby and the use or intended use of the proceeds of the loan proceeds except for liabilities, obligations, losses, damages, penalties, actions, judgments, suits, claims, costs, expenses and disbursements caused by any Indemnified Person's gross negligence or willful misconduct.

12.3 Time of Essence. Time is of the essence for the performance of all Obligations in this Agreement.

12.4 Severability of Provisions. Each provision of this Agreement is severable from every other provision in determining the enforceability of any provision.

12.5 Correction of Loan Documents. Collateral Agent and the Lenders may correct patent errors and fill in any blanks in this Agreement and the other Loan Documents consistent with the agreement of the parties so long as Collateral Agent provides Borrower with written notice of such correction and allows Borrower at least ten (10) days to object to such correction. In the event of such objection, such correction shall not be made except by an amendment signed by both Collateral Agent, the Required Lenders or Lender (as applicable) and Borrower.

12.6 Amendments in Writing; Integration. (a) No amendment, modification, termination or waiver of any provision of this Agreement or any other Loan Document, no approval or consent thereunder, or any consent to any departure by Borrower or any of its Subsidiaries therefrom, shall in any event be effective unless the same shall be in writing and signed by Borrower, Collateral Agent and the Required Lenders provided that:

(i) no such amendment, waiver or other modification that would have the effect of increasing or reducing a Lender's Term Loan Commitment or Commitment Percentage shall be effective as to such Lender without such Lender's written consent;

(ii) no such amendment, waiver or modification that would affect the rights and duties of Collateral Agent shall be effective without Collateral Agent's written consent or signature;

(iii) no such amendment, waiver or other modification shall, unless signed by all the Lenders directly affected thereby, (A) reduce the principal of, rate of interest on or any fees with respect to any Term Loan or forgive any principal, interest (other than default interest) or fees (other than late charges) with respect to any Term Loan (B) postpone the date fixed for, or waive, any payment of principal of any Term Loan or of interest on any Term Loan (other than default interest) or any fees provided for hereunder (other than late charges or for any termination of any commitment); (C) change the definition of the term "**Required Lenders**" or the percentage of Lenders which shall be required for the Lenders to take any action hereunder; (D) release all or substantially all of any material portion of the Collateral, authorize Borrower to sell or otherwise dispose of all or substantially all or any material portion of the Collateral or release any Guarantor of all or any portion of the Obligations or its guaranty obligations with respect thereto, except, in each case with respect to this clause (D), as otherwise may be expressly permitted under this Agreement or the other Loan Documents (including in connection

with any disposition permitted hereunder); (E) amend, waive or otherwise modify this Section 12.6 or the definitions of the terms used in this Section 12.6 insofar as the definitions affect the substance of this Section 12.6; (F) consent to the assignment, delegation or other transfer by Borrower of any of its rights and obligations under any Loan Document or release Borrower of its payment obligations under any Loan Document, except, in each case with respect to this clause (F), pursuant to a merger or consolidation permitted pursuant to this Agreement; (G) amend any of the provisions of Section 9.4 or amend any of the definitions of Pro Rata Share, Term Loan Commitment, Commitment Percentage or that provide for the Lenders to receive their Pro Rata Shares of any fees, payments, setoffs or proceeds of Collateral hereunder; (H) subordinate the Liens granted in favor of Collateral Agent securing the Obligations; or (I) amend any of the provisions of Section 12.10. It is hereby understood and agreed that all Lenders shall be deemed directly affected by an amendment, waiver or other modification of the type described in the preceding clauses (C), (D), (E), (F), (G) and (H) of the preceding sentence;

(iv) the provisions of the foregoing clauses (i), (ii) and (iii) are subject to the provisions of any interlender or agency agreement among the Lenders and Collateral Agent pursuant to which any Lender may agree to give its consent in connection with any amendment, waiver or modification of the Loan Documents only in the event of the unanimous agreement of all Lenders.

(b) Other than as expressly provided for in Section 12.6(a)(i)-(iii), Collateral Agent may, if requested by the Required Lenders, from time to time designate covenants in this Agreement less restrictive by notification to a representative of Borrower.

(c) This Agreement and the Loan Documents represent the entire agreement about this subject matter and supersede prior negotiations or agreements. All prior agreements, understandings, representations, warranties, and negotiations between the parties about the subject matter of this Agreement and the Loan Documents merge into this Agreement and the Loan Documents.

12.7 Counterparts. This Agreement may be executed in any number of counterparts and by different parties on separate counterparts, each of which, when executed and delivered, is an original, and all taken together, constitute one Agreement.

12.8 Survival. All covenants, representations and warranties made in this Agreement continue in full force and effect until this Agreement has terminated pursuant to its terms and all Obligations (other than inchoate indemnity or reimbursement obligations and any other obligations which, by their terms, are to survive the termination of this Agreement) have been satisfied. Without limiting the foregoing, except as otherwise provided in Section 4.1, the grant of security interest by Borrower in Section 4.1 shall survive until the termination of all Bank Services Agreements. The obligation of Borrower in Section 12.2 to indemnify each Lender and Collateral Agent, as well as the confidentiality provisions in Section 12.9 below, shall survive until the statute of limitations with respect to such claim or cause of action shall have run.

12.9 Confidentiality. In handling any confidential information of Borrower, the Lenders and Collateral Agent shall exercise the same degree of care that it exercises for their own proprietary information, but disclosure of information may be made: (a) subject to the terms and conditions of this Agreement, to the Lenders' and Collateral Agent's Subsidiaries or Affiliates, or in connection with a Lender's own financing or securitization transactions and upon the occurrence of a default, event of default or similar occurrence with respect to such financing or securitization transaction; (b) to prospective transferees (other than those identified in (a) above) or purchasers of any interest in the Credit Extensions (provided, however, the Lenders and Collateral Agent shall, except upon the occurrence and during the continuance of an Event of Default, obtain such prospective transferee's or purchaser's agreement to the terms of this provision or to similar, no less restrictive confidentiality terms); (c) as required by law, regulation, subpoena, or other order; (d) to Lenders' or Collateral Agent's regulators or as otherwise required in connection with an examination or audit; (e) as Collateral Agent reasonably considers appropriate in exercising remedies under the Loan Documents; and (f) to third party service providers of the Lenders and/or Collateral Agent so long as such service providers have executed a confidentiality agreement with the Lenders and Collateral Agent with terms no less restrictive than those contained herein. Confidential information does not include information that either: (i) is in the public domain or in the Lenders' and/or Collateral Agent's possession when disclosed to the Lenders and/or Collateral Agent, or becomes part of the public domain after disclosure to the Lenders and/or Collateral Agent (other than as a result of its disclosure by Lenders in violation of this Agreement); or (ii) is disclosed to the Lenders and/or Collateral Agent by a third party, if the Lenders and/or

Collateral Agent does not know that the third party is prohibited from disclosing the information. Subject to the foregoing, Collateral Agent and the Lenders may use confidential information for any purpose, including, without limitation, for the development of client databases, reporting purposes, and market analysis. The provisions of the immediately preceding sentence shall survive the termination of this Agreement. The agreements provided under this Section 12.9 supersede all prior agreements, understanding, representations, warranties, and negotiations between the parties about the subject matter of this Section 12.9.

12.10 Right of Set Off. Borrower hereby grants to Collateral Agent and to each Lender, a lien, security interest and right of set off as security for all Obligations to Collateral Agent and each Lender hereunder, whether now existing or hereafter arising upon and against all deposits, credits, collateral and property, now or hereafter in the possession, custody, safekeeping or control of Collateral Agent or the Lenders or any entity under the control of Collateral Agent or the Lenders (including a Collateral Agent affiliate) or in transit to any of them. At any time after the occurrence and during the continuance of an Event of Default, without demand or notice, Collateral Agent or the Lenders may set off the same or any part thereof and apply the same to any liability or obligation of Borrower even though unmatured and regardless of the adequacy of any other collateral securing the Obligations. ANY AND ALL RIGHTS TO REQUIRE COLLATERAL AGENT TO EXERCISE ITS RIGHTS OR REMEDIES WITH RESPECT TO ANY OTHER COLLATERAL WHICH SECURES THE OBLIGATIONS, PRIOR TO EXERCISING ITS RIGHT OF SETOFF WITH RESPECT TO SUCH DEPOSITS, CREDITS OR OTHER PROPERTY OF BORROWER ARE HEREBY KNOWINGLY, VOLUNTARILY AND IRREVOCABLY WAIVED.

12.11 Public Announcement. Borrower hereby agrees that Collateral Agent and each Lender may make a public announcement of the transactions contemplated by this Agreement, and may publicize the same in marketing materials, newspapers and other publications, and otherwise, and in connection therewith may use Borrower's name, tradenames and logos. Subject to the requirements of Section 12.9, Collateral Agent and the Lenders may also make disclosures to the Securities and Exchange Commission or other governmental agency and any other public disclosure with investors, other governmental agencies or other related persons.

12.12 Cooperation of Borrower. If necessary, Borrower agrees to execute any documents (including new Secured Promissory Notes) reasonably required to effectuate and acknowledge each assignment of a Term Loan Commitment or Loan to an assignee in accordance with Section 12.1. Subject to the provisions of Section 12.9, Borrower authorizes each Lender to disclose to any prospective participant or assignee of a Term Loan Commitment, any and all information in such Lender's possession concerning Borrower and its financial affairs which has been delivered to such Lender by or on behalf of Borrower pursuant to this Agreement, or which has been delivered to such Lender by or on behalf of Borrower in connection with such Lender's credit evaluation of Borrower prior to entering into this Agreement.

12.13 Collateral Agent and Lender Agreement. Collateral Agent and the Lenders hereby agree to the terms and conditions set forth on Annex I attached hereto. Borrower acknowledges and agrees to the terms and conditions set forth on Annex I attached hereto.

13. DEFINITIONS

13.1 Definitions. As used in this Agreement, the following terms have the following meanings:

"**Account**" is any "account" as defined in the Code with such additions to such term as may hereafter be made, and includes, without limitation, all accounts receivable and other sums owing to Borrower.

"**Account Debtor**" is any "account debtor" as defined in the Code with such additions to such term as may hereafter be made.

"**Affiliate**" of any Person is a Person that owns or controls directly or indirectly the Person, any Person that controls or is controlled by or is under common control with the Person, and each of that Person's senior executive officers, directors, partners and, for any Person that is a limited liability company, that Person's managers and members.

"**Agreement**" is defined in the preamble hereof.

* Confidential information, indicated [***], has been omitted from this filing and filed separately with the Securities and Exchange Commission.

"**Amortization Date**" is, December 1, 2017; provided that, if Borrower requests the Term B Loan, the "Amortization Date" shall be June 1, 2018.

"**Annual Projections**" is defined in Section 6.2(a).

"**Anti-Terrorism Laws**" are any laws relating to terrorism or money laundering, including Executive Order No. 13224 (effective September 24, 2001), the USA PATRIOT Act, the laws comprising or implementing the Bank Secrecy Act, and the laws administered by OFAC.

"**Approved Fund**" is any (i) investment company, fund, trust, securitization vehicle or conduit that is (or will be) engaged in making, purchasing, holding or otherwise investing in commercial loans and similar extensions of credit in the ordinary course of its business or (ii) any Person (other than a natural person) which temporarily warehouses loans for any Lender or any entity described in the preceding clause (i) and that, with respect to each of the preceding clauses (i) and (ii), is administered or managed by (a) a Lender, (b) an Affiliate of a Lender or (c) a Person (other than a natural person) or an Affiliate of a Person (other than a natural person) that administers or manages a Lender.

"**Approved Lender**" is defined in Section 12.1.

"**Bank Services**" are any products, credit services, and/or financial accommodations previously, now, or hereafter provided to Borrower or any of its Subsidiaries by Bank or any Bank Affiliate, including, without limitation, any letters of credit, cash management services (including, without limitation, merchant services, direct deposit of payroll, business credit cards, and check cashing services), interest rate swap arrangements, and foreign exchange services as any such products or services may be identified in Bank's various agreements related thereto (each, a "**Bank Services Agreement**").

"**Bank**" is defined in the preamble hereof.

"**Basic Rate**" is, with respect to the Term Loan, the per annum rate of interest (based on a year of three hundred sixty (360) days) equal to the sum of (a) the Prime Rate, as reported in The Wall Street Journal on the last Business Day of the month that immediately precedes the month in which the interest will accrue, plus (b) four and one-tenth percent (4.10%). Notwithstanding the foregoing, the Basic Rate for the Term Loan for the period from the Effective Date through and including November 30, 2016 shall be seven and three-fifths percent (7.60%).

"**Blocked Person**" is any Person: (a) listed in the annex to, or is otherwise subject to the provisions of, Executive Order No. 13224, (b) a Person owned or controlled by, or acting for or on behalf of, any Person that is listed in the annex to, or is otherwise subject to the provisions of, Executive Order No. 13224, (c) a Person with which any Lender is prohibited from dealing or otherwise engaging in any transaction by any Anti-Terrorism Law, (d) a Person that commits, threatens or conspires to commit or supports "terrorism" as defined in Executive Order No. 13224, or (e) a Person that is named a "specially designated national" or "blocked person" on the most current list published by OFAC or other similar list.

"**Borrower**" is defined in the preamble hereof.

"**Borrower's Books**" are Borrower's or any of its Subsidiaries' books and records including ledgers, federal, and state tax returns, records regarding Borrower's or its Subsidiaries' assets or liabilities, the Collateral, business operations or financial condition, and all computer programs or storage or any equipment containing such information.

"**Business Day**" is any day that is not a Saturday, Sunday or a day on which Collateral Agent is closed.

"**Cash Equivalents**" are (a) marketable direct obligations issued or unconditionally guaranteed by the United States or any agency or any State thereof having maturities of not more than one (1) year from the date of acquisition; (b) commercial paper maturing no more than one (1) year after its creation and having the highest rating from either Standard & Poor's Ratings Group or Moody's Investors Service, Inc., (c) certificates of deposit maturing no more than one (1) year after issue, and (d) money market funds at least ninety-five percent (95%) of the assets of which constitute Cash Equivalents of the kinds described in (a) through (c) of this definition. For the avoidance of

doubt, the direct purchase by Borrower or any of its Subsidiaries of any Auction Rate Securities, or purchasing participations in, or entering into any type of swap or other derivative transaction, or otherwise holding or engaging in any ownership interest in any type of Auction Rate Security by Borrower or any of its Subsidiaries shall be conclusively determined by the Lenders as an ineligible Cash Equivalent, and any such transaction shall expressly violate each other provision of this Agreement governing Permitted Investments. Notwithstanding the foregoing, Cash Equivalents does not include and Borrower, and each of its Subsidiaries, are prohibited from purchasing, purchasing participations in, entering into any type of swap or other equivalent derivative transaction, or otherwise holding or engaging in any ownership interest in any type of debt instrument, including, without limitation, any corporate or municipal bonds with a long-term nominal maturity for which the interest rate is reset through a dutch auction and more commonly referred to as an auction rate security (each, an "**Auction Rate Security**").

"**Change in Control**" means any event, transaction, or occurrence as a result of which (a) any "person" (as such term is defined in Sections 3(a)(9) and 13(d)(3) of the Exchange Act), other than a trustee or other fiduciary holding securities under an employee benefit plan of Borrower, is or becomes a beneficial owner (within the meaning Rule 13d-3 promulgated under the Exchange Act), directly or indirectly, of securities of Borrower, representing thirty-five percent (35%) or more of the combined voting power of Borrower's then outstanding securities other than by the sale of Borrower's equity securities in a public offering; or (b) during any period of twelve consecutive calendar months, individuals who at the beginning of such period constituted the Board of Directors of Borrower (together with any new directors whose election by the Board of Directors of Borrower was approved by a vote of not less than a majority of the directors then still in office who either were directions at the beginning of such period or whose election or nomination for election was previously so approved) cease for any reason other than death or disability to constitute a majority of the directors then in office.

"**Claims**" are defined in Section 12.2.

"**Code**" is the Uniform Commercial Code, as the same may, from time to time, be enacted and in effect in the State of New York; provided, that, to the extent that the Code is used to define any term herein or in any Loan Document and such term is defined differently in different Articles or Divisions of the Code, the definition of such term contained in Article or Division 9 shall govern; provided further, that in the event that, by reason of mandatory provisions of law, any or all of the attachment, perfection, or priority of, or remedies with respect to, Collateral Agent's Lien on any Collateral is governed by the Uniform Commercial Code in effect in a jurisdiction other than the State of New York, the term "Code" shall mean the Uniform Commercial Code as enacted and in effect in such other jurisdiction solely for purposes of the provisions thereof relating to such attachment, perfection, priority, or remedies and for purposes of definitions relating to such provisions.

"**Collateral**" is any and all properties, rights and assets of Borrower described on Exhibit A.

"**Collateral Account**" is any Deposit Account, Securities Account, or Commodity Account, or any other bank account maintained by Borrower or any Subsidiary that is a guarantor at any time.

"**Collateral Agent**" is, Bank, not in its individual capacity, but solely in its capacity as agent on behalf of and for the benefit of the Lenders.

"**Collateral Assignment Agreement**" means that certain Consent to Security Interest and Assignment of License Agreement, dated as of the Effective Date between Borrower and Collateral Agent, in form and substance reasonably satisfactory to Collateral Agent and the Initial Lenders.

"**Commitment Percentage**" is set forth in Schedule 1.1, as amended from time to time.

"**Commodity Account**" is any "commodity account" as defined in the Code with such additions to such term as may hereafter be made.

"**Communication**" is defined in Section 10.

"**Compliance Certificate**" is that certain certificate in the form attached hereto as Exhibit C.

"**Contingent Obligation**" is, for any Person, any direct or indirect liability, contingent or not, of that Person for (a) any indebtedness, lease, dividend, letter of credit or other obligation of another such as an obligation directly or indirectly guaranteed, endorsed, co-made, discounted or sold with recourse by that Person, or for which that Person is directly or indirectly liable; (b) any obligations for undrawn letters of credit for the account of that Person; and (c) all obligations from any interest rate, currency or commodity swap agreement, interest rate cap or collar agreement, or other agreement or arrangement designated to protect a Person against fluctuation in interest rates, currency exchange rates or commodity prices; but "Contingent Obligation" does not include endorsements in the ordinary course of business. The amount of a Contingent Obligation is the stated or determined amount of the primary obligation for which the Contingent Obligation is made or, if not determinable, the maximum reasonably anticipated liability for it determined by the Person in good faith; but the amount may not exceed the maximum of the obligations under any guarantee or other support arrangement.

"**Control Agreement**" is any control agreement entered into among the depository institution at which Borrower or any of its Subsidiaries maintains a Deposit Account or the securities intermediary or commodity intermediary at which Borrower or any of its Subsidiaries maintains a Securities Account or a Commodity Account, Borrower and such Subsidiary, and Collateral Agent pursuant to which Collateral Agent obtains control (within the meaning of the Code) for the benefit of the Lenders over such Deposit Account, Securities Account, or Commodity Account.

"**Copyrights**" are any and all copyright rights, copyright applications, copyright registrations and like protections in each work or authorship and derivative work thereof, whether published or unpublished and whether or not the same also constitutes a trade secret.

"**Credit Extension**" is any Term Loan or any other extension of credit by Collateral Agent or Lenders for Borrower's benefit.

"**Default Rate**" is defined in Section 2.3(b).

"**Deposit Account**" is any "deposit account" as defined in the Code with such additions to such term as may hereafter be made.

"**Designated Deposit Account**" is Borrower's deposit account, account number **[_____]**, maintained with Bank.

"**Disbursement Letter**" is that certain form attached hereto as Exhibit B-1.

"**DOJ**" means the U.S. Department of Justice or any successor thereto or any other comparable Governmental Authority.

"**Dollar Equivalent**" is, at any time, (a) with respect to any amount denominated in Dollars, such amount, and (b) with respect to any amount denominated in a Foreign Currency, the equivalent amount therefor in Dollars as determined by Bank at such time on the basis of the then-prevailing rate of exchange in San Francisco, California, for sales of the Foreign Currency for transfer to the country issuing such Foreign Currency.

"**Dollars**," "**dollars**" and "$" each mean lawful money of the United States.

"**Effective Date**" is defined in the preamble of this Agreement.

"**Eligible Assignee**" is (i) a Lender, (ii) an Affiliate of a Lender, (iii) an Approved Fund and (iv) any commercial bank, savings and loan association or savings bank or any other entity which is an "accredited investor" (as defined in Regulation D under the Securities Act of 1933, as amended) and which extends credit or buys loans as one of its businesses, including insurance companies, mutual funds, lease financing companies and commercial finance companies, in each case, which either (A) has a rating of BBB or higher from Standard & Poor's Rating Group and a rating of Baa2 or higher from Moody's Investors Service, Inc. at the date that it becomes a Lender or (B) has total assets in excess of Five Billion Dollars ($5,000,000,000.00), and in each case of clauses (i) through (iv), which, through its applicable lending office, is capable of lending to Borrower without the imposition of any withholding or similar taxes; provided that notwithstanding the foregoing, "Eligible Assignee" shall not include,

unless an Event of Default has occurred and is continuing, (i) Borrower or any of Borrower's Affiliates or Subsidiaries or (ii) a direct competitor of Borrower or a vulture hedge fund, each as determined by Collateral Agent. Notwithstanding the foregoing, (x) in connection with assignments by a Lender due to a forced divestiture at the request of any regulatory agency, the restrictions set forth herein shall not apply and Eligible Assignee shall mean any Person or party and (y) in connection with a Lender's own financing or securitization transactions, the restrictions set forth herein shall not apply and Eligible Assignee shall mean any Person or party providing such financing or formed to undertake such securitization transaction and any transferee of such Person or party upon the occurrence of a default, event of default or similar occurrence with respect to such financing or securitization transaction; provided that no such sale, transfer, pledge or assignment under this clause (y) shall release such Lender from any of its obligations hereunder or substitute any such Person or party for such Lender as a party hereto until Collateral Agent shall have received and accepted an effective assignment agreement from such Person or party in form satisfactory to Collateral Agent executed, delivered and fully completed by the applicable parties thereto, and shall have received such other information regarding such Eligible Assignee as Collateral Agent reasonably shall require.

"**Equipment**" is all "equipment" as defined in the Code with such additions to such term as may hereafter be made, and includes without limitation all machinery, fixtures, goods, vehicles (including motor vehicles and trailers), and any interest in any of the foregoing.

"**Equity Event**" is the receipt by Borrower on or after the Effective Date of unrestricted (including not subject to any clawback, redemption, escrow or similar contractual restriction and otherwise not deemed restricted under GAAP) net cash proceeds of not less than Thirty Million Dollars ($30,000,000.00) from any combination of (i) the issuance and sale by Borrower of its common stock and (ii) "up front" payments in connection with a joint venture, collaboration or other partnering or business development transaction, in each case on terms and conditions reasonably satisfactory to Lenders.

"**ERISA**" is the Employee Retirement Income Security Act of 1974, as amended, and its regulations.

"**Exigent Circumstance**" means any event or circumstance that, in the reasonable judgment of Collateral Agent, imminently threatens the ability of Collateral Agent to realize upon all or any material portion of the Collateral, such as, without limitation, fraudulent removal, concealment, or abscondment thereof, destruction or material waste thereof, or failure of Borrower or any of its Subsidiaries after reasonable demand to maintain or reinstate adequate casualty insurance coverage, or which, in the judgment of Collateral Agent, could reasonably be expected to result in a material diminution in value of the Collateral.

"**Existing Indebtedness**" is the indebtedness of Borrower to SVB in the aggregate principal outstanding amount as of the Effective Date of Two Million Five Hundred Seventy Nine Thousand Seven Hundred Eighty Six Dollars and Fifty One Cents ($2,579,786.51) pursuant to that certain Loan and Security Agreement, dated April 25, 2012 entered into by and between SVB and Borrower.

"**Event of Default**" is defined in Section 8.

"**FDA**" means the U.S. Food and Drug Administration or any successor thereto or any other comparable Governmental Authority.

"**Final Payment**" is a payment (in addition to and not a substitution for the regular monthly payments of principal plus accrued interest) due on the earliest to occur of (a) the Maturity Date, or (b) the acceleration of any Term Loan, or (c) the prepayment of a Term Loan pursuant to Section 2.2(c) or (d), equal to the original principal amount of such Term Loan multiplied by the Final Payment Percentage, payable to Lenders in accordance with their respective Pro Rata Shares.

"**Final Payment Percentage**" is eight and three quarters percent (8.75%).

"**Foreign Currency**" means lawful money of a country other than the United States.

"**Foreign Subsidiary**" is a Subsidiary that is not an entity organized under the laws of the United States or any territory thereof.

"**Funding Date**" is any date on which a Credit Extension is made to or on account of Borrower which shall be a Business Day.

"**FX Contract**" is any foreign exchange contract by and between Borrower and Bank under which Borrower commits to purchase from or sell to Bank a specific amount of Foreign Currency on a specified date.

"**GAAP**" is generally accepted accounting principles set forth in the opinions and pronouncements of the Accounting Principles Board of the American Institute of Certified Public Accountants and statements and pronouncements of the Financial Accounting Standards Board or in such other statements by such other Person as may be approved by a significant segment of the accounting profession in the United States, which are applicable to the circumstances as of the date of determination.

"**General Intangibles**" are all "general intangibles" as defined in the Code in effect on the date hereof with such additions to such term as may hereafter be made, and includes without limitation, all copyright rights, copyright applications, copyright registrations and like protections in each work of authorship and derivative work, whether published or unpublished, any patents, trademarks, service marks and, to the extent permitted under applicable law, any applications therefor, whether registered or not, any trade secret rights, including any rights to unpatented inventions, payment intangibles, royalties, contract rights, goodwill, franchise agreements, purchase orders, customer lists, route lists, telephone numbers, domain names, claims, income and other tax refunds, security and other deposits, options to purchase or sell real or personal property, rights in all litigation presently or hereafter pending (whether in contract, tort or otherwise), insurance policies (including without limitation key man, property damage, and business interruption insurance), payments of insurance and rights to payment of any kind.

"**Governmental Approval**" is any consent, authorization, approval, order, license, franchise, permit, certificate, accreditation, registration, filing or notice, of, issued by, from or to, or other act by or in respect of, any Governmental Authority.

"**Governmental Authority**" is any nation or government, any state or other political subdivision thereof, any agency, authority, instrumentality, regulatory body (including, without limitation, the FDA), court, central bank or other entity exercising executive, legislative, judicial, taxing, regulatory or administrative functions of or pertaining to government, any securities exchange and any self-regulatory organization.

"**Guarantor**" is any Person providing a Guaranty in favor of Collateral Agent.

"**Guaranty**" is any guarantee of all or any part of the Obligations, as the same may from time to time be amended, restated, modified or otherwise supplemented.

"**Indebtedness**" is (a) indebtedness for borrowed money or the deferred price of property or services, such as reimbursement and other obligations for surety bonds and letters of credit, (b) obligations evidenced by notes, bonds, debentures or similar instruments, (c) capital lease obligations, and (d) Contingent Obligations.

"**Indemnified Person**" is defined in Section 12.2.

"**Initial Lender**" means each of Silicon Valley Bank and Solar Capital Ltd.

"**Insolvency Proceeding**" is any proceeding by or against any Person under the United States Bankruptcy Code, or any other bankruptcy or insolvency law, including assignments for the benefit of creditors, compositions, extensions generally with its creditors, or proceedings seeking reorganization, arrangement, or other relief.

"**Insolvent**" means not Solvent.

"**Intellectual Property**" means all of Borrower's or any Subsidiary's right, title and interest in and to the following:

(a) its Copyrights, Trademarks and Patents;

(b) any and all trade secrets and trade secret rights, including, without limitation, any rights to unpatented inventions, know-how, operating manuals;

(c) any and all source code;

(d) any and all design rights;

(e) any and all claims for damages by way of past, present and future infringement of any of the foregoing, with the right, but not the obligation, to sue for and collect such damages for said use or infringement of the Intellectual Property rights identified above; and

(f) all amendments, renewals and extensions of any of the Copyrights, Trademarks or Patents.

"**Inventory**" is all "inventory" as defined in the Code in effect on the date hereof with such additions to such term as may hereafter be made, and includes without limitation all merchandise, raw materials, parts, supplies, packing and shipping materials, work in process and finished products, including without limitation such inventory as is temporarily out of any Person's custody or possession or in transit and including any returned goods and any documents of title representing any of the above.

"**Investment**" is any beneficial ownership interest in any Person (including stock, partnership interest or other securities), and any loan, advance, payment or capital contribution to any Person.

"**Lender**" is any one of the Lenders.

"**Lenders**" are the Persons identified on Schedule 1.1 hereto and each assignee that becomes a party to this Agreement pursuant to Section 12.1.

"**Lenders' Expenses**" are all reasonable documented out-of-pocket audit fees and expenses, costs, and expenses (including reasonable documented out-of-pocket attorneys' fees and expenses, as well as appraisal fees, fees incurred on account of lien searches, inspection fees, and filing fees) for preparing, amending, negotiating, administering, defending and enforcing the Loan Documents (including, without limitation, those incurred in connection with appeals or Insolvency Proceedings) or otherwise incurred by Collateral Agent and/or the Lenders in connection with the Loan Documents.

"**Letter of Credit"** is a standby or commercial letter of credit issued by Bank upon request of Borrower based upon an application, guarantee, indemnity, or similar agreement.

"**Lien**" is a claim, mortgage, deed of trust, levy, charge, pledge, security interest, or other encumbrance of any kind, whether voluntarily incurred or arising by operation of law or otherwise against any property.

"**Loan Documents**" are, collectively, this Agreement, the Warrants, the Perfection Certificates, each Compliance Certificate, each Disbursement Letter, each Loan Payment/Advance Request Form and any Bank Services Agreement, the Collateral Assignment Agreement, any subordination agreements, any note, or notes or guaranties executed by Borrower or any other Person, and any other present or future agreement entered into by Borrower, any Guarantor or any other Person for the benefit of the Lenders and Collateral Agent in connection with this Agreement; all as amended, restated, or otherwise modified.

"**Loan Payment/Advance Request Form**" is that certain form attached hereto as Exhibit B-2.

"**Material Adverse Change**" is (a) a material impairment in the perfection or priority of Collateral Agent's Lien in the Collateral or in the value of such Collateral; (b) a material adverse change in the business, operations or condition (financial or otherwise) of Borrower and Borrower and its Subsidiaries, taken as a whole; or (c) a material impairment of the prospect of repayment of any portion of the Obligations.

"**Maturity Date**" is, for each Term Loan, November 18, 2020.

"**Obligations**" are all of Borrower's obligations to pay when due any debts, principal, interest, Lenders' Expenses, the Prepayment Fee, the Final Payment, the Term B Loan Non-Usage Fee, the Term C Loan Non-Usage Fee, and other amounts Borrower owes the Lenders now or later, in connection with, related to, following, or arising from, out of or under, this Agreement or, the other Loan Documents (other than the Warrants), or otherwise, including, without limitation, all obligations relating to letters of credit (including reimbursement obligations for drawn and undrawn letters of credit), cash management services, and foreign exchange contracts, if any, and including interest accruing after Insolvency Proceedings begin (whether or not allowed) and debts, liabilities, or obligations of Borrower assigned to the Lenders and/or Collateral Agent, and the performance of Borrower's duties under the Loan Documents (other than the Warrants).

"**OFAC**" is the U.S. Department of Treasury Office of Foreign Assets Control.

"**OFAC Lists**" are, collectively, the Specially Designated Nationals and Blocked Persons List maintained by OFAC pursuant to Executive Order No. 13224, 66 Fed. Reg. 49079 (Sept. 25, 2001) and/or any other list of terrorists or other restricted Persons maintained pursuant to any of the rules and regulations of OFAC or pursuant to any other applicable Executive Orders.

"**Operating Documents**" are, for any Person, such Person's formation documents, as certified by the Secretary of State (or equivalent agency) of such Person's jurisdiction of organization on a date that is no earlier than thirty (30) days prior to the Effective Date, and, (a) if such Person is a corporation, its bylaws in current form, (b) if such Person is a limited liability company, its limited liability company agreement (or similar agreement), and (c) if such Person is a partnership, its partnership agreement (or similar agreement), each of the foregoing with all current amendments or modifications thereto.

"**Pangu**" is Pangu Biopharma Limited, an entity organized under the laws of Hong Kong and a subsidiary of Borrower.

"**Patents**" means all patents, patent applications and like protections including without limitation improvements, divisions, continuations, renewals, reissues, extensions and continuations-in-part of the same.

"**Payment Date**" is the first (1st) calendar day of each calendar month, commencing on December 1, 2016.

"**Perfection Certificate**" and "**Perfection Certificates**" is defined in Section 5.1.

"**Permitted Indebtedness**" is:

(a) Borrower's Indebtedness to the Lenders and Collateral Agent under this Agreement and the other Loan Documents;

(b) Indebtedness existing on the Effective Date and disclosed on the Perfection Certificate(s);

(c) Subordinated Debt;

(d) unsecured Indebtedness to trade creditors incurred in the ordinary course of business;

(e) Indebtedness consisting of capitalized lease obligations and purchase money Indebtedness, in each case incurred by Borrower or any of its Subsidiaries to finance the acquisition, repair, improvement or construction of fixed or capital assets of such person, provided that (i) the aggregate outstanding principal amount of all such Indebtedness does not exceed Two Hundred Fifty Thousand Dollars ($250,000.00) at any time and (ii) the principal amount of such Indebtedness does not exceed the lower of the cost or fair market value of the property so acquired or built or of such repairs or improvements financed with such Indebtedness (each measured at the time of such acquisition, repair, improvement or construction is made);

(f) Indebtedness incurred as a result of endorsing negotiable instruments received in the ordinary course of Borrower's business; and

(g) unsecured reimbursement obligations in connection with corporate credit cards, not to exceed Two Hundred Fifty Thousand Dollars ($250,000.00);

(h) unsecured Indebtedness to trade creditors incurred in the ordinary course of business and not past due;

(i) Indebtedness in respect of netting services, overdraft protections and otherwise in connection with deposit accounts;

(j) Indebtedness consisting of financing of insurance premiums in the ordinary course of business not to exceed One Hundred Thousand Dollars ($100,000.00);

(k) unsecured Intercompany Indebtedness between Borrower and its Subsidiaries other than Pangu not to exceed Two Hundred Fifty Thousand Dollars ($250,000.00);

(l) unsecured Indebtedness not otherwise permitted hereunder not to exceed Two Hundred Fifty Thousand Dollars ($250,000.00) at any time outstanding; and

(m) extensions, refinancings, modifications, amendments and restatements of any items of Permitted Indebtedness (a) through (l) above, provided that the principal amount thereof is not increased or the terms thereof are not modified to impose materially more burdensome terms upon Borrower, or its Subsidiary, as the case may be.

"**Permitted Investments**" are:

(a) Investments disclosed on the Perfection Certificate(s) and existing on the Effective Date;

(b) (i) Investments consisting of cash and Cash Equivalents, and (ii) any other Investments permitted by Borrower's investment policy, as amended from time to time, provided that such investment policy (and any such amendment thereto) has been approved in writing by Collateral Agent;

(c) Investments consisting of the endorsement of negotiable instruments for deposit or collection or similar transactions in the ordinary course of Borrower;

(d) Investments consisting of deposit accounts in which Collateral Agent has a perfected security interest to the extent required under this Agreement;

(e) Investments in connection with Transfers permitted by Section 7.1;

(f) Investments by Borrower in Subsidiaries other than Pangu not to exceed Two Hundred Fifty Thousand Dollars ($250,000.00) in the aggregate in any fiscal year;

(g) Investments consisting of (i) travel advances and employee relocation loans and other employee loans and advances in the ordinary course of business, and (ii) loans to employees, officers or directors relating to the purchase of equity securities of Borrower or its Subsidiaries pursuant to employee stock purchase plans or agreements approved by Borrower's Board of Directors;

(h) Investments (including debt obligations) received in connection with the bankruptcy or reorganization of customers or suppliers and in settlement of delinquent obligations of, and other disputes with, customers or suppliers arising in the ordinary course of business;

(i) Investments consisting of notes receivable of, or prepaid royalties and other credit extensions, to customers and suppliers who are not Affiliates, in the ordinary course of business; provided that this paragraph shall not apply to Investments of Borrower in any Subsidiary; and

(j) non-cash Investments in joint ventures or strategic alliances in the ordinary course of Borrower's business consisting of the non-exclusive licensing of technology, the development of technology or the providing of technical support;

(k) Investments (i) by Borrower or Subsidiaries that are guarantors in Borrower or Subsidiaries that are guarantors and (ii) by Borrower or Subsidiaries that are guarantors in Subsidiaries that are not Pangu and not guarantors in an amount not to exceed Two Hundred Fifty Thousand Dollars ($250,000.00) in the aggregate in any fiscal year; and

(l) Other Investments not otherwise permitted hereunder not to exceed Two Hundred Fifty Thousand Dollars ($250,000.00) in the aggregate in any fiscal year.

"**Permitted Licenses**" are (A) licenses of over-the-counter software that is commercially available to the public, and (B) non-exclusive licenses for the use of the Intellectual Property of Borrower or any of its Subsidiaries entered into in the ordinary course of business and licenses that could not result in a legal transfer of the licensed property but that may be exclusive as to territory only as to discrete geographical areas outside of the United States.

"**Permitted Liens**" are:

(a) Liens existing on the Effective Date and disclosed on the Perfection Certificates or arising under this Agreement and the other Loan Documents;

(b) Liens for taxes, fees, assessments or other government charges or levies, either (i) not due and payable or (ii) being contested in good faith and for which Borrower maintains adequate reserves on its Books, provided that no notice of any such Lien has been filed or recorded under the Internal Revenue Code of 1986, as amended, and the Treasury Regulations adopted thereunder;

(c) liens securing Indebtedness permitted under clause (e) of the definition of "**Permitted Indebtedness**," provided that (i) such liens exist prior to the acquisition of, or attach substantially simultaneous with, or within twenty (20) days after the, acquisition, lease, repair, improvement or construction of, such property financed or leased by such Indebtedness and (ii) such liens do not extend to any property of Borrower other than the property (and proceeds thereof) acquired, leased or built, or the improvements or repairs, financed by such Indebtedness;

(d) Liens of carriers, warehousemen, suppliers, or other Persons that are possessory in nature arising in the ordinary course of business so long as such Liens attach only to Inventory, and which are not delinquent or remain payable without penalty or which are being contested in good faith and by appropriate proceedings which proceedings have the effect of preventing the forfeiture or sale of the property subject thereto;

(e) Liens to secure payment of workers' compensation, employment insurance, old-age pensions, social security and other like obligations incurred in the ordinary course of business (other than Liens imposed by ERISA);

(f) Liens incurred in the extension, renewal or refinancing of the indebtedness secured by Liens described in (a) through (c), but any extension, renewal or replacement Lien must be limited to the property encumbered by the existing Lien and the principal amount of the indebtedness may not increase;

(g) leases or subleases of real property granted in the ordinary course of Borrower's business (or, if referring to another Person, in the ordinary course of such Person's business), and leases, subleases, non-exclusive licenses or sublicenses of personal property (other than Intellectual Property) granted in the ordinary course of Borrower's business (or, if referring to another Person, in the ordinary course of such Person's business), if the leases, subleases, licenses and sublicenses do not prohibit granting Collateral Agent or any Lender a security interest therein;

(h) banker's liens, rights of setoff and Liens in favor of financial institutions incurred in the ordinary course of business arising in connection with Borrower's deposit accounts or securities accounts held at

such institutions solely to secure payment of fees and similar costs and expenses and provided such accounts are maintained in compliance with Section 6.6(b) hereof;

(i) Liens arising from judgments, decrees or attachments in circumstances not constituting an Event of Default under Section 8.4 or 8.7;

(j) Liens consisting of Permitted Licenses;

(k) Liens in favor of other financial institutions arising in connection with Borrower's deposit and/or securities accounts held at such institutions;

(l) Liens on insurance proceeds in favor of insurance companies granted solely to secured financed insurance premiums not to exceed One Hundred Thousand Dollars ($100,000.00); and

(m) other Liens not otherwise permitted hereunder securing indebtedness not to exceed Two Hundred Fifty Thousand Dollars ($250,000.00).

"**Person**" is any individual, sole proprietorship, partnership, limited liability company, joint venture, company, trust, unincorporated organization, association, corporation, institution, public benefit corporation, firm, joint stock company, estate, entity or government agency.

"**Prepayment Fee**" is, with respect to any Term Loan subject to prepayment prior to the Maturity Date, whether by mandatory or voluntary prepayment, acceleration or otherwise, an additional fee payable to the Lenders in amount equal to:

(i) for a prepayment made on or after the Effective Date up to but not including the first anniversary of the Effective Date, three percent (3.00%) of the principal amount of the Term Loans prepaid;

(ii) for a prepayment made after the date on or after the first anniversary of the Effective Date up to but not including the second anniversary of the Effective Date, two percent (2.00%) of the principal amount of the Term Loans prepaid;

(iii) for a prepayment made on or after the date which is after the second anniversary of the Effective Date, one percent (1.00%) of the principal amount of the Term Loans prepaid.

"**Pro Rata Share**" is, as of any date of determination, with respect to each Lender, a percentage (expressed as a decimal, rounded to the ninth decimal place) determined by dividing the outstanding principal amount of Term Loans held by such Lender by the aggregate outstanding principal amount of all Term Loans.

"**Registered Organization**" is any "registered organization" as defined in the Code with such additions to such term as may hereafter be made.

"**Registration**" means any registration, authorization, approval, license, permit, clearance, certificate, and exemption issued or allowed by the FDA or state pharmacy licensing authorities (including, without limitation, new drug applications, abbreviated new drug applications, biologics license applications, investigational new drug applications, over-the-counter drug monograph, device pre-market approval applications, device pre-market notifications, investigational device exemptions, product recertifications, manufacturing approvals, registrations and authorizations, CE Marks, pricing and reimbursement approvals, labeling approvals or their foreign equivalent, controlled substance registrations, and wholesale distributor permits).

"**Regulatory Action**" means an administrative, regulatory, or judicial enforcement action, proceeding, investigation or inspection, FDA Form 483 notice of inspectional observation, warning letter, untitled letter, other notice of violation letter, recall, seizure, Section 305 notice or other similar written communication, injunction or consent decree, issued by the FDA or a federal or state court.

"**Required Lenders**" means (i) for so long as all of the Persons that are Lenders on the Effective Date (each an "**Original Lender**") have not assigned or transferred any of their interests in their Term Loan, Lenders

holding one hundred percent (100%) of the aggregate outstanding principal balance of the Term Loan, or (ii) at any time from and after any Original Lender has assigned or transferred any interest in its Term Loan, Lenders holding at least sixty six percent (66%) of the aggregate outstanding principal balance of the Term Loan and, in respect of this clause (ii), (A) each Original Lender that has not assigned or transferred any portion of its Term Loan, (B) each assignee or transferee of an Original Lender's interest in the Term Loan, but only to the extent that such assignee or transferee is an Affiliate or Approved Fund of such Original Lender, and (C) any Person providing financing to any Person described in clauses (A) and (B) above; provided, however, that this clause (C) shall only apply upon the occurrence of a default, event of default or similar occurrence with respect to such financing. Solely with respect to Borrower's notice and delivery requirements hereunder, Borrower shall determine Required Lenders under clause (ii) above based on Lender Transfers for which Borrower has received notice.

"**Requirement of Law**" is as to any Person, the organizational or governing documents of such Person, and any law (statutory or common), treaty, rule or regulation or determination of an arbitrator or a court or other Governmental Authority, in each case applicable to or binding upon such Person or any of its property or to which such Person or any of its property is subject.

"**Responsible Officer**" is any of the President, VP of Finance, Chief Executive Officer, or Chief Financial Officer of Borrower acting alone.

"**Second Draw Period**" is the period commencing on the date Borrower has achieved the Second Draw Period Milestones and ending on the earlier of (i) June 30, 2017 and (ii) the occurrence of an Event of Default; provided, however, that the Second Draw Period shall not commence if on the date of the occurrence of the Second Draw Period Milestones an Event of Default has occurred and is continuing.

"**Second Draw Period Milestones**" is the achievement of each of the following: (i) the Equity Event; (ii) the [***]; and (iii) Borrower's receipt of positive long term safety data on Resolaris in open studies for each of ATYR1940-C-005 and ATYR1940-C-006; each in form and content reasonably acceptable to Collateral Agent and the Lenders.

"**Secured Promissory Note**" is defined in Section 2.4.

"**Secured Promissory Note Record**" is a record maintained by each Lender with respect to the outstanding Obligations owed by Borrower to Lender and credits made thereto.

"**Securities Account**" is any "securities account" as defined in the Code with such additions to such term as may hereafter be made.

"**Shares**" is one hundred percent (100%) of the issued and outstanding capital stock, membership units or other securities owned or held of record by Borrower or Borrower's Subsidiary, in any Subsidiary; provided that, in the event Borrower, demonstrates to Collateral Agent's reasonable satisfaction, that a pledge of more than sixty five percent (65%) of the Shares of such Subsidiary which is a Foreign Subsidiary, creates a present and existing adverse tax consequence to Borrower under the U.S. Internal Revenue Code, "Shares" shall mean sixty-five percent (65%) of the issued and outstanding capital stock, membership units or other securities owned or held of record by Borrower or its Subsidiary in such Foreign Subsidiary.

"**Solvent**" is, with respect to any Person: the fair salable value of such Person's consolidated assets (including goodwill minus disposition costs) exceeds the fair value of such Person's liabilities; such Person is not left with unreasonably small capital after the transactions in this Agreement; and such Person is able to pay its debts (including trade debts) as they mature.

"**Subordinated Debt**" is indebtedness incurred by Borrower or any of its Subsidiaries subordinated to all Indebtedness of Borrower and/or its Subsidiaries to the Lenders (pursuant to a subordination, intercreditor, or other similar agreement in form and substance reasonably satisfactory to Collateral Agent and the Lenders entered into between Collateral Agent, Borrower, and/or any of its Subsidiaries, and the other creditor), on terms reasonably acceptable to Collateral Agent and the Lenders.

* Confidential information, indicated [***], has been omitted from this filing and filed separately with the Securities and Exchange Commission.

"**Subsidiary**" is, with respect to any Person, any Person of which more than fifty percent (50%) of the voting stock or other equity interests (in the case of Persons other than corporations) is owned or controlled, directly or indirectly, by such Person or through one or more intermediaries.

"**Term Loan**" is defined in Section 2.2(a)(iii) hereof.

"**Term A Loan**" is defined in Section 2.2(a)(i) hereof.

"**Term B Loan**" is defined in Section 2.2(a)(ii) hereof.

"**Term B Loan Non-Usage Fee**" is an additional, one-time fee payable to the Lenders, if at all, in amount equal to (i) two percent (2.00%) multiplied by (ii) Five Million Dollars ($5,000,000.00) minus the aggregate amount of Term B Loans requested by Borrower on or before June 30, 2017; provided that the Term B Loan Non-Usage Fee shall be paid, if at all, on the earlier of July 1, 2017 or prior repayment in connection with Sections 2.2(c) or (d), and may be debited (or ACH'd) from any of Borrower's Accounts.

"**Term C Loan**" is defined in Section 2.2(a)(iii) hereof.

"**Term C Loan Non-Usage Fee**" is an additional, one-time fee payable to the Lenders, if at all, in amount equal to (i) two percent (2.00%) multiplied by (ii) Five Million Dollars ($5,000,000.00) minus the aggregate amount of Term C Loans requested by Borrower on or before December 31, 2017; provided that the Term C Loan Non-Usage Fee shall be paid, if at all, on the earlier of January 1, 2018 or prior repayment in connection with Sections 2.2(c) or (d), and may be debited (or ACH'd) from any of Borrower's Accounts.

"**Term Loan Commitment**" is, for any Lender, the obligation of such Lender to make a Term Loan, up to the principal amount shown on Schedule 1.1**.** "**Term Loan Commitments**" means the aggregate amount of such commitments of all Lenders.

"**Third Draw Period**" is the period commencing on the later of (i) June 30, 2017 and (ii) the date Borrower has achieved the Third Draw Period Milestones and ending on the earlier of (i) December 31, 2017 and (ii) the occurrence of an Event of Default; provided, however, that the Third Draw Period shall not commence if on the date of the occurrence of the Third Draw Period Milestones an Event of Default has occurred and is continuing.

"**Third Draw Period Milestones**" is the achievement of each of the following: (i) the Second Draw Period Milestones; (ii) positive Phase 1b/2 interim data readout from Resolaris trial for either (a) adult facioscapulohumoral muscular dystrophy, (b) early onset facioscapulohumoral muscular dystrophy or (c) limb-girdle muscular dystrophy; and (iii) either (x) initiation of "iMod.Fc" Phase 1 clinical trial within the United States or the European Union or (y) either (I) thirty days have elapsed from the Food and Drug Administration's receipt of an exploratory initial investigational new drug application in connection with the iMod.Fc clinical trial (provided, that the achievement of the Third Draw Period Milestones shall not occur in the event of an issuance by the Food and Drug Administration during such thirty day period of notice that such clinical trial is subject to a clinical hold under 21 C.F.R. § 312.42 until the earlier of (A) such time as such clinical hold expires or is otherwise terminated or (B) the Third Draw Period has expired), or (II) evidence of approval from the European Medicines Agency for a clinical trial authorization in connection with the iMod.Fc clinical trial; each in form and content reasonably acceptable to Collateral Agent and the Lenders.

"**Trademarks**" means any trademark and servicemark rights, whether registered or not, applications to register and registrations of the same and like protections, and the entire goodwill of the business of Borrower connected with and symbolized by such trademarks.

"**Transfer**" is defined in Section 7.1.

"**Warrants**" are those certain Warrants to Purchase Stock dated as of the Effective Date, or any date theretofore or thereafter, issued by Borrower in favor of each Lender or such Lender's Affiliates.

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IN WITNESS WHEREOF, the parties hereto have caused this Agreement to be executed as of the Effective Date.

BORROWER:

ATYR PHARMA, INC.

By /s/ John Blake
Name: John Blake
Title: VP, Finance

COLLATERAL AGENT AND LENDER:

SILICON VALLEY BANK

By /s/ Anthony Flores
Name: Anthony Flores
Title: Director

LENDER:

SOLAR CAPTIAL LTD.

By /s/Anthony J. Storino
Name: Anthony J. Storino
Title:Authorized Signtory

SCHEDULE 1.1

Lenders and Commitments

Term A Loans

Lender	Term Loan Commitment	Commitment Percentage
SILICON VALLEY BANK	$5,000,000.00	50.00%
SOLAR CAPITAL LTD.	$5,000,000.00	50.00%
TOTAL	**$10,000,000.00**	**100.00%**

Term B Loans

Lender	Term Loan Commitment	Commitment Percentage
SILICON VALLEY BANK	$2,500,000.00	50.00%
SOLAR CAPITAL LTD.	$2,500,000.00	50.00%
TOTAL	$5,000,000.00	**100.00%**

Term C Loans

Lender	Term Loan Commitment	Commitment Percentage
SILICON VALLEY BANK	$2,500,000.00	50.00%
SOLAR CAPITAL LTD.	$2,500,000.00	50.00%
TOTAL	$5,000,000.00	**100.00%**

Aggregate (all Term Loans)

Lender	Term Loan Commitment	Commitment Percentage
SILICON VALLEY BANK	$10,000,000.00	50.00%
SOLAR CAPITAL LTD.	$10,000,000.00	50.00%
TOTAL	**$20,000,000.00**	**100.00%**

EXHIBIT A

Description of Collateral

The Collateral consists of all of Borrower's right, title and interest in and to the following personal property:

All goods, Accounts (including health-care receivables), Equipment, Inventory, contract rights or rights to payment of money, leases, license agreements, franchise agreements, General Intangibles (except as noted below), commercial tort claims, documents, instruments (including any promissory notes), chattel paper (whether tangible or electronic), cash, deposit accounts and other Collateral Accounts, all certificates of deposit, fixtures, letters of credit rights (whether or not the letter of credit is evidenced by a writing), securities, and all other investment property, supporting obligations, and financial assets, whether now owned or hereafter acquired, wherever located; and

All Borrower's Books relating to the foregoing, and any and all claims, rights and interests in any of the above and all substitutions for, additions, attachments, accessories, accessions and improvements to and replacements, products, proceeds and insurance proceeds of any or all of the foregoing.

Notwithstanding the foregoing, the Collateral does not include (a) more than sixty five percent (65%) of the presently existing and hereafter arising issued and outstanding shares of capital stock owned by Borrower of any Foreign Subsidiary which shares entitle the holder thereof to vote for directors or any other matter, (b) any Intellectual Property; provided, however, the Collateral shall include all Accounts and all proceeds of Intellectual Property or (c) rights held under a license that are not assignable by their terms without the consent of the licensor thereof (but only to the extent such restriction on assignment is enforceable under applicable law). If a judicial authority (including a U.S. Bankruptcy Court) would hold that a security interest in the underlying Intellectual Property is necessary to have a security interest in such Accounts and such property that are proceeds of Intellectual Property, then the Collateral shall automatically, and effective as of the Effective Date, include the Intellectual Property to the extent necessary to permit perfection of Collateral Agent's security interest in such Accounts and such other property of Borrower that are proceeds of the Intellectual Property.

Pursuant to the terms of a certain negative pledge arrangement with Collateral Agent and the Lenders, Borrower has agreed not to encumber any of its Intellectual Property.

EXHIBIT B-1

Form of Disbursement Letter

[see attached]

DISBURSEMENT LETTER

[DATE]

The undersigned, being the duly elected and acting of ATYR PHARMA, INC., a Delaware corporation with an office located at 3545 John Hopkins Court, Suite 250, San Diego, CA 92121 ("**Borrower**"), does hereby certify to **SILICON VALLEY BANK** ("**Bank**" and "**Lender**"), as collateral agent (the "**Collateral Agent**") in connection with that certain Loan and Security Agreement dated as of November 18, 2016, by and among Borrower, Collateral Agent and the Lenders from time to time party thereto (the "**Loan Agreement**"; with other capitalized terms used below having the meanings ascribed thereto in the Loan Agreement) that:

1. The representations and warranties made by Borrower in Section 5 of the Loan Agreement and in the other Loan Documents are true and correct in all material respects as of the date hereof (provided, that those representations and warranties expressly referring to a specific date shall be true and correct in all material respects as of such date).

2. No event or condition has occurred that would constitute an Event of Default under the Loan Agreement or any other Loan Document.

3. Borrower is in compliance with the covenants and requirements contained in Sections 4, 6 and 7 of the Loan Agreement.

4. All conditions referred to in Section 3 of the Loan Agreement to the making of the Loan to be made on or about the date hereof have been satisfied or waived by Collateral Agent.

5. No Material Adverse Change has occurred.

6. The undersigned is a Responsible Officer.

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7. The proceeds of the Term [A][B][C] Loan shall be disbursed as follows:

Disbursement from Bank:	
Loan Amount	$_____
Plus:	
--Deposit Received	$_____
Less:	
--Existing Final Payment Fee	($_____)
--Facility Fee	($_____)
--Existing Debt Payoff to be remitted to SVB per the Payoff Letter dated [DATE]	($_____)]
[--Interim Interest	($_____)]
--Lender's Legal Fees	($_____)*
Net Proceeds due from Solar:	**$_____**
Disbursement from Solar:	
Loan Amount	$_____
Plus:	
--Deposit Received	$_____
Less:	
--Facility Fee	($_____)
[--Interim Interest	($_____)]
--Lender's Legal Fees	($_____)*
Net Proceeds due from Solar:	**$_____**
TOTAL TERM [A][B][C] LOAN NET PROCEEDS FROM LENDERS	**$_____**

8. The [Term Loan][Term A Loan][Term C Loan] shall amortize in accordance with the Amortization Table attached hereto.

9. The aggregate net proceeds of the Term Loans shall be transferred to the Designated Deposit Account as follows:

Account Name: ATYR PHARMA, INC.

Bank Name:

Bank Address:

Account Number:

ABA Number:

[Balance of Page Intentionally Left Blank]

* Legal fees and costs are through the Effective Date. Postclosing legal fees and costs, payable after the Effective Date, to be invoiced and paid postclosing.
* Legal fees and costs are through the Effective Date. Postclosing legal fees and costs, payable after the Effective Date, to be invoiced and paid postclosing.

Dated as of the date first set forth above.

BORROWER:

ATYR PHARMA, INC.

By
Name:
Title:

COLLATERAL AGENT AND LENDER:

SILICON VALLEY BANK

By
Name:
Title:

LENDER:

SOLAR CAPITAL LTD.

By
Name:
Title:

AMORTIZATION TABLE
(Term [A][B][C] Loan)

[see attached]

EXHIBIT B-2

Loan Payment/Advance Request Form

Deadline for same day processing is Noon Pacific Time*

Fax To: Date: November __, 2016

YMENT:

ATYR PHARMA, INC.

ount #_____ To Account #_____
(Deposit Account #) (Loan Account #)
$_____ and/or Interest $_____

l Signature: Phone Number:
e/Title:

VANCE:

Outgoing Wire Request section below if all or a portion of the funds from this loan advance are for an outgoing wire.

ount #_____ To Account #_____
(Loan Account #) (Deposit Account #)

f Advance $_____

ver's representations and warranties in the Loan and Security Agreement are true and correct in all material respects on the date of the request for an advance; provided, however, that such materiality qualifier shall not be to any representations and warranties that already are qualified or modified by materiality in the text thereof; and provided, further that those representations and warranties expressly referring to a specific date shall be rrect in all material respects as of such date:

l Signature: Phone Number:
e/Title:

G WIRE REQUEST:
only if all or a portion of funds from the loan advance above is to be wired.
or same day processing is noon, Pacific Time

r Name: _____ Amount of Wire:

r Bank: _____ Account Number:
tate:

r Bank Transit (ABA) #: Beneficiary Bank Code (Swift, Sort, Chip, etc.):
(For International Wire Only)
ry Bank: Transit (ABA) #:
r Credit to:

truction:
below, I (we) acknowledge and agree that my (our) funds transfer request shall be processed in accordance with and subject to the terms and conditions set forth in the agreements(s) covering funds transfer which agreements(s) were previously received and executed by me (us).

l Signature: _____ 2nd Signature (if required): _____
e/Title: _____ Print Name/Title: _____
#: Telephone #:

EXHIBIT C

Compliance Certificate

TO: SILICON VALLEY BANK, as Collateral Agent and Lender
SOLAR CAPITAL LTD., as Lender

FROM: ATYR PHARMA, INC.

The undersigned authorized officer ("**Officer**") of ATYR PHARMA, INC. (" **Borrower**"), hereby certifies that in accordance with the terms and conditions of the Loan and Security Agreement by and among Borrower, Collateral Agent, and the Lenders from time to time party thereto (the " **Loan Agreement**;" capitalized terms used but not otherwise defined herein shall have the meanings given them in the Loan Agreement),

(a) Borrower is in complete compliance for the period ending _____ with all required covenants except as noted below;

(b) There are no Events of Default, except as noted below;

(c) Except as noted below, all representations and warranties of Borrower stated in the Loan Documents are true and correct in all material respects on this date and for the period described in (a), above; provided, however, that such materiality qualifier shall not be applicable to any representations and warranties that already are qualified or modified by materiality in the text thereof; and provided, further that those representations and warranties expressly referring to a specific date shall be true and correct in all material respects as of such date.

(d) Borrower, and each of Borrower's Subsidiaries, has timely filed all required tax returns and reports, Borrower, and each of Borrower's Subsidiaries, has timely paid all foreign, federal, state, and local taxes, assessments, deposits and contributions owed by Borrower, or Subsidiary, except as otherwise permitted pursuant to the terms of Section 5.8 of the Loan Agreement;

(e) No Liens have been levied or claims made against Borrower or any of its Subsidiaries relating to unpaid employee payroll or benefits of which Borrower has not previously provided written notification to Collateral Agent and the Lenders.

Attached are the required documents, if any, supporting our certification(s). The Officer, on behalf of Borrower, further certifies that the attached financial statements are prepared in accordance with Generally Accepted Accounting Principles (GAAP) and are consistently applied from one period to the next except as explained in an accompanying letter or footnotes and except, in the case of unaudited financial statements, for the absence of footnotes and subject to year-end audit adjustments as to the interim financial statements.

Please indicate compliance status since the last Compliance Certificate by circling Yes, No, or N/A under "Complies" column.

	Reporting Covenant	Requirement	Actual	Complies		
1)	Financial statements	Quarterly within five (5) days after filing with the SEC		Yes	No	N/A
2)	Annual (CPA Audited) statements	Earlier of (x) 180 days after FYE or (y) within five (5) days after filing with the SEC		Yes	No	N/A

3)	Annual Financial Projections/Budget (prepared on a monthly basis)	Annually, within earlier of (i) 60 days after FYE and (ii) 7 days of board approval, and when revised		Yes	No	N/A
4)	A/R & A/P agings	If applicable		Yes	No	N/A
5)	8-K, 10-K and 10-Q Filings	within 5 days of filing		Yes	No	N/A
6)	Compliance Certificate	Quarterly within five (5) days after filing financial statements with the SEC		Yes	No	N/A
7)	Total amount of Borrower's cash and cash equivalents at the last day of the measurement period		$_____			
8)	Total amount of Borrower's Subsidiaries' cash and cash equivalents at the last day of the measurement period		$_____			

Deposit and Securities Accounts
(Please list all accounts; attach separate sheet if additional space needed)

	Institution Name	**Account Number**	**New Account?**		**Account Control Agreement in place?**	
1)			Yes	No	Yes	No
2)			Yes	No	Yes	No
3)			Yes	No	Yes	No
4)			Yes	No	Yes	No

Other Matters

1)	Have there been any changes in any Responsible Officer since the last Compliance Certificate?	Yes	No
2)	Have there been any transfers/sales/disposals/retirement of Collateral or IP prohibited by the Loan Agreement?	Yes	No
3)	Have there been any new or pending claims or causes of action against Borrower that involve more than Two Hundred Fifty Thousand Dollars ($250,000.00)?	Yes	No
4)	Have there been any amendments of or other changes to the capitalization table of Borrower and to the Operating Documents of Borrower or any of its Subsidiaries? If yes, provide copies of any such amendments or changes with this Compliance Certificate.	Yes	No

Exceptions

Please explain any exceptions with respect to the certification above: (If no exceptions exist, state "No exceptions." Attach separate sheet if additional space needed.)

ATYR PHARMA, INC.

By
Name:
Title:

Date:

LENDER USE ONLY

Received by: Date:

Verified by: Date:

Compliance Status: Yes No

EXHIBIT D

Form of Secured Promissory Note

[see attached]

SECURED PROMISSORY NOTE
(Term [A][B][C] Loan)

$_____ Dated: [DATE]

FOR VALUE RECEIVED, the undersigned, ATYR PHARMA, INC., a Delaware corporation with an office located at 3545 John Hopkins Court, Suite 250, San Diego, CA 92121 ("**Borrower**") HEREBY PROMISES TO PAY to the order of [SILICON VALLEY BANK][SOLAR CAPITAL LTD.] ("**Lender**") the principal amount of [_____] MILLION DOLLARS ($_____) or such lesser amount as shall equal the outstanding principal balance of the Term [A][B][C] Loan made to Borrower by Lender, plus interest on the aggregate unpaid principal amount of such Term [A][B][C] Loan, at the rates and in accordance with the terms of the Loan and Security Agreement dated [DATE] by and among Borrower, Lender, Silicon Valley Bank, as Collateral Agent, and the other Lenders from time to time party thereto (as amended, restated, supplemented or otherwise modified from time to time, the "**Loan Agreement**"). If not sooner paid, the entire principal amount and all accrued and unpaid interest hereunder shall be due and payable on the Maturity Date as set forth in the Loan Agreement. Any capitalized term not otherwise defined herein shall have the meaning attributed to such term in the Loan Agreement.

Principal, interest and all other amounts due with respect to the Term [A][B][C] Loan, are payable in lawful money of the United States of America to Lender as set forth in the Loan Agreement and this Secured Promissory Note (this "**Note**"). The principal amount of this Note and the interest rate applicable thereto, and all payments made with respect thereto, shall be recorded by Lender and, prior to any transfer hereof, endorsed on the grid attached hereto which is part of this Note.

The Loan Agreement, among other things, (a) provides for the making of a secured Term [A][B][C] Loan by Lender to Borrower, and (b) contains provisions for acceleration of the maturity hereof upon the happening of certain stated events.

This Note may not be prepaid except as set forth in Section 2.2 (c) and Section 2.2(d) of the Loan Agreement.

This Note and the obligation of Borrower to repay the unpaid principal amount of the Term [A][B][C] Loan, interest on the Term [A][B][C] Loan and all other amounts due Lender under the Loan Agreement is secured under the Loan Agreement.

Presentment for payment, demand, notice of protest and all other demands and notices of any kind in connection with the execution, delivery, performance and enforcement of this Note are hereby waived.

Borrower shall pay all reasonable documented fees and expenses, including, without limitation, reasonable documented attorneys' fees and costs, incurred by Lender in the enforcement or attempt to enforce any of Borrower's obligations hereunder not performed when due.

This Note shall be governed by, and construed and interpreted in accordance with, the internal laws of the State of New York.

The ownership of an interest in this Note shall be registered on a record of ownership maintained by Lender or its agent. Notwithstanding anything else in this Note to the contrary, the right to the principal of, and stated interest on, this Note may be transferred only if the transfer is registered on such record of ownership and the transferee is identified as the owner of an interest in the obligation. Borrower shall be entitled to treat the registered holder of this Note (as recorded on such record of ownership) as the owner in fact thereof for all purposes and shall not be bound to recognize any equitable or other claim to or interest in this Note on the part of any other person or entity.

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IN WITNESS WHEREOF, Borrower has caused this Note to be duly executed by one of its officers thereunto duly authorized on the date hereof.

BORROWER:

ATYR PHARMA, INC.

By
Name:
Title:

LOAN INTEREST RATE AND PAYMENTS OF PRINCIPAL

Date	Principal Amount	Interest Rate	Scheduled Payment Amount	Notation By

CORPORATE BORROWING CERTIFICATE

Borrower: ATYR PHARMA, INC. **Date**: November __, 2016
Lenders: SILICON VALLEY BANK, as Collateral Agent and Lender
SOLAR CAPITAL LTD., as Lender

I hereby certify as follows, as of the date set forth above:

1. I am the Secretary, Assistant Secretary or other officer of Borrower. My title is as set forth below.

2. Borrower's exact legal name is set forth above. Borrower is a corporation existing under the laws of the State of Delaware.

3. Attached hereto as Exhibit A and Exhibit B, respectively, are true, correct and complete copies of (i) Borrower's Articles/Certificate of Incorporation (including amendments), as filed with the Secretary of State of the state in which Borrower is incorporated as set forth in paragraph 2 above; and (ii) Borrower's Bylaws. Neither such Articles/Certificate of Incorporation nor such Bylaws have been amended, annulled, rescinded, revoked or supplemented, and such Articles/Certificate of Incorporation and such Bylaws remain in full force and effect as of the date hereof.

4. The following resolutions were duly and validly adopted by Borrower's Board of Directors at a duly held meeting of such directors (or pursuant to a unanimous written consent or other authorized corporate action). Such resolutions are in full force and effect as of the date hereof and have not been in any way modified, repealed, rescinded, amended or revoked, and the Lenders may rely on them until each Lender receives written notice of revocation from Borrower.

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Resolved, that **any one** of the following officers or employees of Borrower, whose names, titles and signatures are below, may act on behalf of Borrower:

Name	Title	Signature	Authorized to Add or Remove Signatories
			☐
			☐
			☐
			☐

Resolved Further, that **any one** of the persons designated above with a checked box beside his or her name may, from time to time, add or remove any individuals to and from the above list of persons authorized to act on behalf of Borrower.

Resolved Further, that such individuals may, on behalf of Borrower:

Borrow Money. Borrow money from the Lenders.
Execute Loan Documents. Execute any loan documents any Lender requires.
Grant Security. Grant Collateral Agent a security interest in any of Borrower's assets.
Negotiate Items. Negotiate or discount all drafts, trade acceptances, promissory notes, or other indebtedness in which Borrower has an interest and receive cash or otherwise use the proceeds.
Issue Warrants. Issue warrants for Borrower's capital stock.
Further Acts. Designate other individuals to request advances, pay fees and costs and execute other documents or agreements (including documents or agreement that waive Borrower's right to a jury trial) they believe to be necessary to effectuate such resolutions.

Resolved Further, that all acts authorized by the above resolutions and any prior acts relating thereto are ratified.

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5. The persons listed above are Borrower's officers or employees with their titles and signatures shown next to their names.

By:

Name:

Title:

**** If the Secretary, Assistant Secretary or other certifying officer executing above is designated by the resolutions set forth in paragraph 4 as one of the authorized signing officers, this Certificate must also be signed by a second authorized officer or director of Borrower.*

I, the _____ of Borrower, hereby certify as to paragraphs 1 through 5 above, as
[print title]
of the date set forth above.

By:

Name:

Title:

[*Signature Page to Corporate Borrowing Certificate*]

EXHIBIT A

Certificate of Incorporation (including amendments)

[see attached]

EXHIBIT B

Bylaws

[see attached]

DEBTOR: **ATYR PHARMA, INC.**
SECURED PARTY: **SILICON VALLEY BANK,**
as Collateral Agent

EXHIBIT A TO UCC FINANCING STATEMENT

Description of Collateral

The Collateral consists of all of Debtor's right, title and interest in and to the following personal property:

All goods, Accounts (including health-care receivables), Equipment, Inventory, contract rights or rights to payment of money, leases, license agreements, franchise agreements, General Intangibles (except as noted below), commercial tort claims, documents, instruments (including any promissory notes), chattel paper (whether tangible or electronic), cash, deposit accounts and other Collateral Accounts, all certificates of deposit, fixtures, letters of credit rights (whether or not the letter of credit is evidenced by a writing), securities, and all other investment property, supporting obligations, and financial assets, whether now owned or hereafter acquired, wherever located; and

All Debtor's Books relating to the foregoing, and any and all claims, rights and interests in any of the above and all substitutions for, additions, attachments, accessories, accessions and improvements to and replacements, products, proceeds and insurance proceeds of any or all of the foregoing.

Notwithstanding the foregoing, the Collateral does not include (a) more than sixty five percent (65%) of the presently existing and hereafter arising issued and outstanding shares of capital stock owned by Debtor of any Foreign Subsidiary which shares entitle the holder thereof to vote for directors or any other matter or (b) any Intellectual Property; provided, however, the Collateral shall include all Accounts and all proceeds of Intellectual Property. If a judicial authority (including a U.S. Bankruptcy Court) would hold that a security interest in the underlying Intellectual Property is necessary to have a security interest in such Accounts and such property that are proceeds of Intellectual Property, then the Collateral shall automatically, and effective as of the Effective Date, include the Intellectual Property to the extent necessary to permit perfection of Collateral Agent's security interest in such Accounts and such other property of Debtor that are proceeds of the Intellectual Property.

Pursuant to the terms of a certain negative pledge arrangement with Collateral Agent and the Lenders, Debtor has agreed not to encumber any of its Intellectual Property.

Capitalized terms used but not defined herein have the meanings ascribed in the Uniform Commercial Code in effect in the State of California as in effect from time to time (the "Code") or, if not defined in the Code, then in the Loan and Security Agreement by and between Debtor, Secured Party and the other Lenders party thereto (as modified, amended and/or restated from time to time).

Marketing Consent Form

SVB Financial Group is proud of our business relationships and occasionally likes to promote these relationships. We would like to use your company's information and logo for promotional and marketing purposes in SVB Financial Group member businesses (collectively "SVB") materials. While we would appreciate your consent to all of the uses listed below, please review and select all of the uses that you consent to below.

Indicate your selection(s) by checking the boxes below

☐ **Marketing**: You consent to SVB's use of Company's name, logo and images provided to us in written and oral presentations, advertising, marketing and PR materials, professional lists and websites.

☐ **Deal Terms:** You consent to SVB's inclusion of the size and type of any loan or credit facility alongside your company's name in any oral presentations, advertising, marketing and PR materials, customer lists, and websites.

☐ **Reference:** You consent to SVB's use of Company and representatives' names as a reference for SVB.

☐ **Testimonial:** You consent to SVB's use of Company and representatives' names and quotations in written and oral presentations, marketing and PR materials, and websites. Our practice is to send you a draft of any quotation concerning Company prior to publishing.

☐ 75565057721500 **News release:** You consent to SVB's use of Company's name, trademarks, service marks, quotations and images provided to us in the SVB's news releases concerning Company. Our practice is to send you a draft of any news release concerning Company prior to publishing.

In order to maintain the integrity of your logos, please provide them in:
- Full color and black and white versions, with or without taglines
- At least 300 dpi in PNG, EPS, TIF, or JPG formats (please do not send PDF or website logos).

Please make sure to print the Company name, and any individual names and titles as you would like them displayed in materials or lists.

Company name	
Additional names	

You grant to SVB a limited license to use the information for the limited purposes above, which you can revoke upon written notice to SVB. The signer below acknowledges that he or she has authority to bind the Company to this consent. SVB will not be responsible for versions that were printed prior to receiving notice revoking any such consent. Company is solely responsible for defense and maintenance of its intellectual property.

Please contact your Relationship Advisor or SVB representative if you have any questions.

Accepted or Agreed on Behalf Of Company or Yourself			
Name		Title	
Signature		Today's date	
Address			
Phone number		Email	

Return this completed form and any attachments to your Relationship Advisor or SVB via email at logo@svb.com.

ANNEX I

Collateral Agent and Lender Terms

1. Appointment of Collateral Agent.

a. Each Lender hereby appoints the Bank (together with any successor Collateral Agent pursuant to Section 7 of this Annex I) as Collateral Agent under the Loan Documents and authorizes Collateral Agent to (i) execute and deliver the Loan Documents and accept delivery thereof on its behalf from Borrower, (ii) take such action on its behalf and to exercise all rights, powers and remedies and perform the duties as are expressly delegated to Collateral Agent under such Loan Documents and (iii) exercise such powers as are reasonably incidental thereto.

b. Without limiting the generality of clause (a) above, Collateral Agent shall have the sole and exclusive right and authority (to the exclusion of the Lenders), and is hereby authorized, to (i) act as the disbursing and collecting agent for the Lenders with respect to all payments and collections arising in connection with the Loan Documents (including in any other bankruptcy, insolvency or similar proceeding), and each Person making any payment in connection with any Loan Document to any Lender is hereby authorized to make such payment to Collateral Agent except to the extent the Loan Documents specifically require a payment to be made directly to a Lender, (ii) file and prove claims and file other documents necessary or desirable to allow the claims of Collateral Agent and Lenders with respect to any Obligation in any bankruptcy, insolvency or similar proceeding (but not to vote, consent or otherwise act on behalf of such Lender), (iii) act as collateral agent for the Lenders for purposes of the perfection of all Liens created by the Loan Documents and all other purposes stated therein, (iv) manage, supervise and otherwise deal with the Collateral as permitted pursuant to the Loan Agreement, (v) take such other action as is necessary or desirable to maintain the perfection and priority of the Liens created or purported to be created by the Loan Documents, (vi) except as may be otherwise specified in any Loan Document and subject to clause (d) below, exercise all remedies given to Collateral Agent and the other Lenders with respect to Borrower and/or the Collateral, whether under the Loan Documents, applicable Requirements of Law or otherwise and (vii) execute any amendment, consent or waiver under the Loan Documents on behalf of any Lender that has consented in writing to such amendment, consent or waiver, all of the foregoing actions to be taken in Collateral Agent's reasonable business discretion; provided, however, that Collateral Agent hereby appoints, authorizes and directs each Lender to act as collateral sub-agent for Collateral Agent and the Lenders for purposes of the perfection of all Liens with respect to the Collateral, including any Deposit Account maintained by Borrower or any Guarantor with, and cash and Cash Equivalents held by, such Lender, and may further authorize and direct the Lenders to take further actions as collateral sub-agents for purposes of enforcing such Liens or otherwise to transfer the Collateral subject thereto to Collateral Agent, and each Lender hereby agrees to take such further actions to the extent, and only to the extent, so authorized and directed. Collateral Agent may, upon any term or condition it specifies, delegate or exercise any of its rights, powers and remedies under, and delegate or perform any of its duties or any other action with respect to, any Loan Document by or through any trustee, co-agent, employee, attorney-in-fact and any other Person (including any Lender). Any such Person shall benefit from this Annex I to the extent provided by Collateral Agent.

c. Under the Loan Documents, and except as expressly set forth in this Annex I, Collateral Agent (i) is acting solely on behalf of the Lenders, with duties that are entirely administrative in nature, notwithstanding the use of the defined term "Collateral Agent", the terms "agent", "Collateral Agent" and "collateral agent" and similar terms in any Loan Document to refer to Collateral Agent, which terms are used for title purposes only, (ii) is not assuming any obligation under any Loan Document other than as expressly set forth therein or any role as agent, fiduciary or trustee of or for any Lender or any other Person and (iii) shall have no implied functions, responsibilities, duties, obligations or other liabilities under any Loan Document, and each Lender, by accepting the benefits of the Loan Documents, hereby waives and agrees not to assert any claim against Collateral Agent based on the roles, duties and legal relationships expressly disclaimed in clauses (i) through (iii) above. Except as expressly set forth in the Loan Documents, Collateral Agent shall not have any duty to disclose, and shall not be liable for failure to disclose, any information relating to Borrower or any of its Subsidiaries that is communicated to or obtained by the Bank or any of its Affiliates in any capacity.

d. Upon the occurrence of an Event of Default, Collateral Agent, at the request of Required Lenders, shall take such actions and only such actions as Lenders mutually agree to take to enforce Collateral

Agent's and their rights and remedies under the Loan Agreement, provided, that, notwithstanding anything to the contrary contained in the foregoing or anything else in this Agreement, unless Collateral Agent shall have received an objection or contrary instructions from the other Lender, Collateral Agent may take such actions (not to include acceleration of the Loan Agreement, the institution of foreclosure proceedings or secured creditors' sales or the giving of notice to any account debtors) as Collateral Agent shall deem reasonably necessary to preserve and protect the rights of Collateral Agent and Lenders under the Loan Agreement and the other Loan Documents and with respect to the Collateral, including without limitation satisfaction of other security interests, liens or encumbrances on the Collateral not permitted under the Loan Documents, payment of taxes on behalf of Borrower, payments to landlords, warehouseman, bailees and other persons in possession of the Collateral and other actions to protect and safeguard the Collateral, and actions with respect to insurance claims for casualty events affecting Borrower and/or the Collateral. If, after consultation, Lenders cannot mutually agree on what action to take or direct Collateral Agent to take, then the other Lender shall have the right upon prior written notice to the other to cause the acceleration of the Loan Agreement on behalf of both Lenders. Upon such acceleration, the Lenders shall mutually agree as to what Enforcement Action to take; provided, however, that if after consultation, Lenders cannot mutually agree on what action to take, then the Lender wishing to take the stronger Enforcement Action (the "Enforcing Lender") shall have the right to determine and shall control the timing, order and type of Enforcement Actions which will be taken and all other matters in connection with any such Enforcement Actions. To facilitate these rights to control Enforcement Actions, upon either Lender becoming the Enforcing Lender, if the Enforcing Lender is not already the Collateral Agent, then automatically and without the necessity of any further action being taken by any party, (x) the original Collateral Agent shall be deemed to have resigned as Collateral Agent and (y) the Lenders shall be deemed to have unanimously appointed the Enforcing Lender as successor Collateral Agent under this Agreement and the Loan Documents (and the Enforcing Lender shall be deemed to have accepted such appointment) in accordance with Section 7 of this Annex, provided, that, once the Enforcing Lender shall have been appointed as the Collateral Agent under the provisions of this sentence, the Enforcing Lender as such successor Collateral Agent shall no longer be bound by the restrictions of the first sentence of this paragraph, but instead shall have the right to determine and control all Enforcement Actions as provided for in the immediately preceding sentence (subject to the provisions of the following sentence). In taking such Enforcement Actions pursuant to the previous sentence, the Enforcing Lender as such successor Collateral Agent shall act reasonably and in good faith and shall consult with and keep the other Lender informed thereof at reasonable intervals; provided, however, that notwithstanding any such consultations and provision of information to the other Lender, the Enforcing Lender as such successor Collateral Agent shall retain the right to make all determinations in the event of disagreements between the Enforcing Lender and the other Lender. In all cases with respect to Enforcement Actions, the Enforcing Lender shall have the right to act both on its own behalf and as agent for the other Lender with respect thereto. In addition, the other Lender shall take such actions and execute such documents and instruments as the Enforcing Lender may reasonably request in connection with and to facilitate any such Enforcement Actions. As used herein, "Enforcement Action" means, with respect to any Lender and with respect to any Claim of such Lender or any item of Collateral in which such Lender has or claims a security interest, lien or right of offset, any action, whether judicial or nonjudicial, to repossess, collect, accelerate, offset, recoup, give notification to third parties with respect to, sell, dispose of, foreclose upon, give notice of sale, disposition, or foreclosure with respect to, or obtain equitable or injunctive relief with respect to, such Claim or Collateral. The filing by any Lender of, or the joining in the filing by any Lender of, an involuntary bankruptcy or insolvency proceeding against Borrower also is an Enforcement Action. Notwithstanding anything herein to the contrary, this clause (d) only applies and only grants rights to Bank and Solar.

2. Binding Effect; Use of Discretion; E-Systems.

a. Each Lender, by accepting the benefits of the Loan Documents, agrees that (i) any action taken by Collateral Agent or the Required Lenders (or, if expressly required in any Loan Document, a greater proportion of the Lenders) in accordance with the provisions of the Loan Documents, (ii) any action taken by Collateral Agent in reliance upon the instructions of the Required Lenders (or, where so required, such greater proportion) and (iii) the exercise by Collateral Agent or the Required Lenders (or, where so required, such greater proportion) of the powers set forth herein or therein, together with such other powers as are reasonably incidental thereto, shall be authorized and binding upon all of Lenders.

b. If Collateral Agent shall request instructions from the Required Lenders or all affected Lenders with respect to any act or action (including failure to act) in connection with any Loan Document, then Collateral Agent shall be entitled to refrain from such act or taking such action unless and until Collateral Agent

shall have received instructions from the Required Lenders or all affected Lenders, as the case may be, and Collateral Agent shall not incur liability to any Person by reason of so refraining. Collateral Agent shall be fully justified in failing or refusing to take any action under any Loan Document (i) if such action would, in the opinion of Collateral Agent, be contrary to any Requirement of Law or any Loan Document, (ii) if such action would, in the opinion of Collateral Agent, expose Collateral Agent to any potential liability under any Requirement of Law or (iii) if Collateral Agent shall not first be indemnified to its satisfaction against any and all liability and expense which may be incurred by it by reason of taking or continuing to take any such action. Without limiting the foregoing, no Lender shall have any right of action whatsoever against Collateral Agent as a result of Collateral Agent acting or refraining from acting under any Loan Document in accordance with the instructions of the Required Lenders or all affected Lenders, as applicable.

c. Collateral Agent is hereby authorized by Borrower and each Lender to establish procedures (and to amend such procedures from time to time) to facilitate administration and servicing of the Term Loans and other matters incidental thereto. Without limiting the generality of the foregoing, Collateral Agent is hereby authorized to establish procedures to make available or deliver, or to accept, notices, documents (including, without limitation, borrowing base certificates) and similar items on, by posting to or submitting and/or completion, on E-Systems. Borrower and each Lender acknowledges and agrees that the use of transmissions via an E-System or electronic mail is not necessarily secure and that there are risks associated with such use, including risks of interception, disclosure and abuse, and Borrower and each Lender assumes and accepts such risks by hereby authorizing the transmission via E-Systems or electronic mail. Each "e signature" on any such posting shall be deemed sufficient to satisfy any requirement for a "signature", and each such posting shall be deemed sufficient to satisfy any requirement for a "writing", in each case including pursuant to any Loan Document, any applicable provision of any Code, the federal Uniform Electronic Transactions Act, the Electronic Signatures in Global and National Commerce Act and any substantive or procedural Requirement of Law governing such subject matter. All uses of an E-System shall be governed by and subject to, in addition to this Section, the separate terms, conditions and privacy policy posted or referenced in such E-System (or such terms, conditions and privacy policy as may be updated from time to time, including on such E-System) and related contractual obligations executed by Collateral Agent, Borrower and/or Lenders in connection with the use of such E-System. ALL E-SYSTEMS AND ELECTRONIC TRANSMISSIONS SHALL BE PROVIDED "AS IS" AND "AS AVAILABLE". NO REPRESENTATION OR WARRANTY OF ANY KIND IS MADE BY AGENT, ANY LENDER OR ANY OF THEIR RELATED PERSONS IN CONNECTION WITH ANY E SYSTEMS.

3. Collateral Agent's Reliance, Etc. Collateral Agent may, without incurring any liability hereunder, (a) consult with any of its Related Persons and, whether or not selected by it, any other advisors, accountants and other experts (including advisors to, and accountants and experts engaged by, Borrower) and (b) rely and act upon any document and information (including those transmitted by electronic transmission) and any telephone message or conversation, in each case believed by it in good faith to be genuine and transmitted, signed or otherwise authenticated by the appropriate parties. None of Collateral Agent and its Related Persons shall be liable for any action taken or omitted to be taken by any of them in connection with the duties of Collateral Agent under or in connection with any Loan Document, and each Lender and Borrower hereby waives and shall not assert (and Borrower shall cause its Subsidiaries to waive and agree not to assert) any right, claim or cause of action based thereon, except to the extent of liabilities resulting from the gross negligence or willful misconduct of Collateral Agent or, as the case may be, such Related Person (each as determined in a final, non-appealable judgment of a court of competent jurisdiction) in connection with the duties of Collateral Agent expressly set forth herein. Without limiting the foregoing, Collateral Agent: (i) shall not be responsible or otherwise incur liability for any action or omission taken in reliance upon the instructions of the Required Lenders or for the actions or omissions of any of its Related Persons, except to the extent that a court of competent jurisdiction determines in a final non-appealable judgment that Collateral Agent acted with gross negligence or willful misconduct in the selection of such Related Person; (ii) shall not be responsible to any Lender or other Person for the due execution, legality, validity, enforceability, effectiveness, genuineness, sufficiency or value of, or the attachment, perfection or priority of any Lien created or purported to be created under or in connection with, any Loan Document; (iii) makes no warranty or representation, and shall not be responsible, to any Lender or other Person for any statement, document, information, representation or warranty made or furnished by or on behalf of Borrower or any Related Person of Borrower in connection with any Loan Document or any transaction contemplated therein or any other document or information with respect to Borrower, whether or not transmitted or (except for documents expressly required under any Loan Document to be transmitted to the Lenders) omitted to be transmitted by Collateral Agent, including as to

completeness, accuracy, scope or adequacy thereof, or for the scope, nature or results of any due diligence performed by Collateral Agent in connection with the Loan Documents; and (iv) shall not have any duty to ascertain or to inquire as to the performance or observance of any provision of any Loan Document, whether any condition set forth in any Loan Document is satisfied or waived, as to the financial condition of Borrower or as to the existence or continuation or possible occurrence or continuation of any Event of Default, and shall not be deemed to have notice or knowledge of such occurrence or continuation unless it has received a notice from Borrower or any Lender describing such Event of Default that is clearly labeled "notice of default" (in which case Collateral Agent shall promptly give notice of such receipt to all Lenders.

4. Collateral Agent Individually. To the extent Collateral Agent or any of its Affiliates becomes a Lender hereunder, it shall have and may exercise the same rights and powers hereunder and shall be subject to the same obligations and liabilities as any other Lender and the terms "Lender", "Required Lender" and any similar terms shall, except where otherwise expressly provided in any Loan Document, include, without limitation, Collateral Agent or such Affiliate, as the case may be, in its individual capacity as Lender, or as one of the Required Lenders.

5. Lender Credit Decision; Collateral Agent Report. Each Lender acknowledges that it shall, independently and without reliance upon Collateral Agent, any Lender or any of their Related Persons or upon any document solely or in part because such document was transmitted by Collateral Agent or any of its Related Persons, conduct its own independent investigation of the financial condition and affairs of Borrower and make and continue to make its own credit decisions in connection with entering into, and taking or not taking any action under, any Loan Document or with respect to any transaction contemplated in any Loan Document, in each case based on such documents and information as it shall deem appropriate. Except for documents expressly required by any Loan Document to be transmitted by Collateral Agent to the Lenders, Collateral Agent shall not have any duty or responsibility to provide any Lender with any credit or other information concerning the business, prospects, operations, Property, financial and other condition or creditworthiness of Borrower or any Affiliate of Borrower that may come in to the possession of Collateral Agent or any of its Related Persons. Each Lender agrees that is shall not rely on any field examination, audit or other report provided by Collateral Agent or its Related Persons (a "Collateral Agent Report"). Each Lender further acknowledges that any Collateral Agent Report (a) is provided to the Lenders solely as a courtesy, without consideration, and based upon the understanding that such Lender will not rely on such Collateral Agent Report, (b) was prepared by Collateral Agent or its Related Persons based upon information provided by Borrower solely for Collateral Agent's own internal use, and (c) may not be complete and may not reflect all information and findings obtained by Collateral Agent or its Related Persons regarding the operations and condition of Borrower. Neither Collateral Agent nor any of its Related Persons makes any representations or warranties of any kind with respect to (i) any existing or proposed financing, (ii) the accuracy or completeness of the information contained in any Collateral Agent Report or in any related documentation, (iii) the scope or adequacy of Collateral Agent's and its Related Persons' due diligence, or the presence or absence of any errors or omissions contained in any Collateral Agent Report or in any related documentation, and (iv) any work performed by Collateral Agent or Collateral Agent's Related Persons in connection with or using any Collateral Agent Report or any related documentation. Neither Collateral Agent nor any of its Related Persons shall have any duties or obligations in connection with or as a result of any Lender receiving a copy of any Collateral Agent Report. Without limiting the generality of the forgoing, neither Collateral Agent nor any of its Related Persons shall have any responsibility for the accuracy or completeness of any Collateral Agent Report, or the appropriateness of any Collateral Agent Report for any Lender's purposes, and shall have no duty or responsibility to correct or update any Collateral Agent Report or disclose to any Lender any other information not embodied in any Collateral Agent Report, including any supplemental information obtained after the date of any Collateral Agent Report. Each Lender releases, and agrees that it will not assert, any claim against Collateral Agent or its Related Persons that in any way relates to any Collateral Agent Report or arises out of any Lender having access to any Collateral Agent Report or any discussion of its contents, and agrees to indemnify and hold harmless Collateral Agent and its Related Persons from all claims, liabilities and expenses relating to a breach by any Lender arising out of such Lender's access to any Collateral Agent Report or any discussion of its contents.

6. Indemnification. Each Lender agrees to reimburse Collateral Agent and each of its Related Persons (to the extent not reimbursed by Borrower as required under the Loan Documents (including pursuant to Section 12.2 of the Agreement)) promptly upon demand for its Pro Rata Share of any reasonable out-of-pocket costs and expenses (including, without limitation, reasonable fees, charges and disbursements of financial, legal and other

advisors and any taxes or insurance paid in the name of, or on behalf of, Borrower) incurred by Collateral Agent or any of its Related Persons in connection with the preparation, syndication, execution, delivery, administration, modification, amendment, consent, waiver or enforcement of, or the taking of any other action (whether through negotiations, through any work-out, bankruptcy, restructuring or other legal or other proceeding (including, without limitation, preparation for and/or response to any subpoena or request for document production relating thereto) or otherwise) in respect of, or legal advice with respect to, its rights or responsibilities under, any Loan Document (collectively, "Costs"); provided that no Lender shall be liable for the payment to Collateral Agent of any Costs which resulted from the gross negligence or willful misconduct of Collateral Agent or, as the case may be, such Related Person, as determined by a final non-appealable judgment of a court of competent jurisdiction. Each Lender further agrees to indemnify Collateral Agent and each of its Related Persons (to the extent not reimbursed by Borrower as required under the Loan Documents (including pursuant to Section 12.2 of the Agreement)), ratably according to its Pro Rata Share, from and against any and all liabilities, obligations, losses, damages, penalties, actions, judgments, suits, costs, expenses or disbursements of any kind or nature whatsoever (including, to the extent not indemnified by the applicable Lender, taxes, interests and penalties imposed for not properly withholding or backup withholding on payments made to or for the account of any Lender) that may be imposed on, incurred by, or asserted against Collateral Agent or any of its Related Persons in any matter relating to or arising out of, in connection with or as a result of any Loan Document or any other act, event or transaction related, contemplated in or attendant to any such document, or, in each case, any action taken or omitted to be taken by Collateral Agent or any of its Related Persons under or with respect to the foregoing; provided that no Lender shall be liable to Collateral Agent or any of its Related Persons under this Section 6 of this Annex I to the extent such liability has resulted from the gross negligence or willful misconduct of Collateral Agent or, as the case may be, such Related Person, as determined by a final non-appealable judgment of a court of competent jurisdiction.

7. Successor Collateral Agent. Collateral Agent may resign at any time by delivering notice of such resignation to the Lenders and Borrower, effective on the date set forth in such notice or, if no such date is set forth therein, upon the date such notice shall be effective, in accordance with the terms of this Section 7 of this Annex I. If Collateral Agent delivers any such notice, the Required Lenders shall have the right to appoint a successor Collateral Agent. If, after 30 days after the date of the retiring Collateral Agent's notice of resignation, no successor Collateral Agent has been appointed by the Required Lenders and has accepted such appointment, then the retiring Collateral Agent may, on behalf of the Lenders, appoint a successor Collateral Agent from among the Original Lenders, if any, and if none, from among the Lenders. Effective immediately upon its resignation, (a) the retiring Collateral Agent shall be discharged from its duties and obligations under the Loan Documents, (b) the Lenders shall assume and perform all of the duties of Collateral Agent until a successor Collateral Agent shall have accepted a valid appointment hereunder, (c) the retiring Collateral Agent and its Related Persons shall no longer have the benefit of any provision of any Loan Document other than with respect to any actions taken or omitted to be taken while such retiring Collateral Agent was, or because such Collateral Agent had been, validly acting as Collateral Agent under the Loan Documents, and (d) subject to its rights under Section 2(b) of this Annex I, the retiring Collateral Agent shall take such action as may be reasonably necessary to assign to the successor Collateral Agent its rights as Collateral Agent under the Loan Documents. Effective immediately upon its acceptance of a valid appointment as Collateral Agent, a successor Collateral Agent shall succeed to, and become vested with, all the rights, powers, privileges and duties of the retiring Collateral Agent under the Loan Documents.

8. Release of Collateral. Each Lender hereby consents to the release and hereby directs Collateral Agent to release (or in the case of clause (b)(ii) below, release or subordinate) the following:

a. any Guarantor or co-Borrower if all of the stock of such Subsidiary owned by Borrower is sold or transferred in a transaction permitted under the Loan Documents (including pursuant to a valid waiver or consent), to the extent that, after giving effect to such transaction, such Subsidiary would not be required to guaranty any Obligations pursuant to any Loan Document; and

b. any Lien held by Collateral Agent for the benefit of the Lenders against (i) any Collateral that is sold or otherwise disposed of by Borrower or any Guarantor in a transaction permitted by the Loan Documents (including pursuant to a valid waiver or consent), (ii) any Collateral subject to a Lien that is expressly permitted under clause (c) of the definition of the term "Permitted Lien" and (iii) all of the Collateral, Borrower, and any Guarantor upon (A) termination of all of the Term Loan Commitments, (B) the payment in full in cash of all of the Obligations (other than (a) inchoate indemnity or reimbursement obligations and (b) other obligations that

survive termination of this Agreement, in each case, for which no claim has been made), and (C) to the extent requested by Collateral Agent or a Lender, receipt by Collateral Agent and Lenders of liability releases from Borrower in form and substance acceptable to Collateral Agent and the Lenders (the satisfaction of the conditions in this clause (iii), the "Termination Date").

9. Setoff and Sharing of Payments. In addition to any rights now or hereafter granted under any applicable Requirement of Law and not by way of limitation of any such rights, upon the occurrence and during the continuance of any Event of Default and subject to Section 10(d) of this Annex I, each Lender is hereby authorized at any time or from time to time upon the direction of Collateral Agent, without notice to Borrower or any other Person, any such notice being hereby expressly waived, to setoff and to appropriate and to apply any and all balances held by it at any of its offices for the account of Borrower (regardless of whether such balances are then due to Borrower) and any other properties or assets at any time held or owing by that Lender or that holder to or for the credit or for the account of Borrower against and on account of any of the Obligations that are not paid when due. Any Lender exercising a right of setoff or otherwise receiving any payment on account of the Obligations in excess of its Pro Rata Share thereof shall purchase for cash (and the other Lenders or holders shall sell) such participations in each such other Lender's or holder's Pro Rata Share of the Obligations as would be necessary to cause such Lender to share the amount so offset or otherwise received with each other Lender or holder in accordance with their respective Pro Rata Shares of the Obligations. Borrower agrees, to the fullest extent permitted by law, that (a) any Lender may exercise its right to offset with respect to amounts in excess of its Pro Rata Share of the Obligations and may purchase participations in accordance with the preceding sentence and (b) any Lender so purchasing a participation in the Term Loans made or other Obligations held by other Lenders or holders may exercise all rights of offset, bankers' liens, counterclaims or similar rights with respect to such participation as fully as if such Lender or holder were a direct holder of the Term Loans and the other Obligations in the amount of such participation. Notwithstanding the foregoing, if all or any portion of the offset amount or payment otherwise received is thereafter recovered from the Lender that has exercised the right of offset, the purchase of participations by that Lender shall be rescinded and the purchase price restored without interest.

10. Advances; Payments; Non-Funding Lenders; Actions in Concert.

a. Advances; Payments. If Collateral Agent receives any payment with respect to the Term Loan for the account of the Lenders on or prior to 2:00 p.m. (New York time) on any Business Day, Collateral Agent shall pay to each applicable Lender such Lender's Pro Rata Share of such payment on such Business Day. If Collateral Agent receives any payment with respect to the Term Loan for the account of Lenders after 2:00 p.m. (New York time) on any Business Day, Collateral Agent shall pay to each applicable Lender such Lender's Pro Rata Share of such payment on the next Business Day.

b. Return of Payments.

i. If Collateral Agent pays an amount to a Lender under this Agreement in the belief or expectation that a related payment has been or will be received by Collateral Agent or on behalf of from Borrower and such related payment is not received by Collateral Agent, then Collateral Agent will be entitled to recover such amount (including interest accruing on such amount at the rate otherwise applicable to such Obligation) from such Lender on demand without setoff, counterclaim or deduction of any kind.

ii. If Collateral Agent determines at any time that any amount received by Collateral Agent under any Loan Document must be returned to Borrower or paid to any other Person pursuant to any insolvency law or otherwise, then, notwithstanding any other term or condition of any Loan Document, Collateral Agent will not be required to distribute any portion thereof to any Lender. In addition, each Lender will repay to Collateral Agent on demand any portion of such amount that Collateral Agent has distributed to such Lender, together with interest at such rate, if any, as Collateral Agent is required to pay to Borrower or such other Person, without setoff, counterclaim or deduction of any kind and Collateral Agent will be entitled to set off against future distributions to such Lender any such amounts (with interest) that are not repaid on demand.

c. Non-Funding Lenders. To the extent that any Lender has failed to fund the Term Loan or any other payments required to be made by it under the Loan Documents after any such Term Loan is required to be made or such payment is due (a "Non-Funding Lender"), Collateral Agent shall be entitled to set off the funding short-fall against that Non-Funding Lender's Pro Rata Share of all payments received from or on behalf of Borrower

thereunder. The failure of any Non Funding Lender to make the Term Loan or any payment required by it hereu nder shall not relieve any other Lender (each such other Lender, an "Other Lender") of its obligations to make such Term Loan, but neither any Other Lender nor Collateral Agent shall be responsible for the failure of any Non-Funding Lender to make such Term Loan or make any other payment required hereunder. Notwithstanding anything set forth herein to the contrary, a Non-Funding Lender shall not have any voting or consent rights under or with respect to any Loan Document or constitute a "Lender" (or be included in the calculation of "Required Lenders" hereunder) for any voting or consent rights under or with respect to any Loan Document. At Borrower's request, Collateral Agent or a Person reasonably acceptable to Collateral Agent shall have the right with Collateral Agent's consent and in Collateral Agent's sole discretion (but Collateral Agent or any such Person shall have no obligation) to purchase from any Non-Funding Lender, and each Lender agrees that if it becomes a Non-Funding Lender it shall, at Collateral Agent's request, sell and assign to Collateral Agent or such Person, all of the Term Loan Commitment (if any), and all of the outstanding Term Loan of that Non-Funding Lender for an amount equal to the aggregate outstanding principal balance of the Term Loan held by such Non-Funding Lender and all accrued interest with respect thereto through the date of sale, such purchase and sale to be consummated pursuant to an executed assignment agreement in form and substance reasonably satisfactory to, and acknowledged by, Collateral Agent.

d. Actions in Concert. Anything in this Agreement to the contrary notwithstanding, each Lender hereby agrees with each other Lender that no Lender shall take any action to protect or enforce its rights arising out of any Loan Document (including exercising any rights of setoff) without first obtaining the prior written consent of the Required Lenders, it being the intent of Lenders that any such action to protect or enforce rights under any Loan Document shall be taken in concert and at the direction or with the consent of the Required Lenders.

Exhibit 10.18

October 23, 2015

Sanuj Ravindran, M.D.

Re: Final Offer of Employment

Dear Sanuj,

This letter is a formal offer setting forth the principal terms for you to join aTyr Pharma, Inc. ("aTyr" or the "Company"), a Delaware corporation, which is located in San Diego, California. This offer is contingent upon the satisfactory completion of a background check.

Position:	Chief Business Officer
Location:	San Diego, CA
Status:	Full-Time, Exempt. This means you are paid for the job and not by the hour. Accordingly, you will not receive overtime pay if you work more than 8 hours in a work day or 40 hours in a workweek.
Reporting to:	John D. Mendlein, Ph.D., Executive Chairman and CEO
Base Salary Rate:	$15,625.00 semi-monthly (which equals $375,000.00 per year) less applicable withholdings, paid in accordance with Company's normal payroll practices during your Full-Time employment. Future adjustments in compensation, if any, will be made by the Company in its sole and absolute discretion.
Sign-On Bonus:	You will be offered a one-time sign-on bonus in the amount of $25,000.00 to be paid at the time of your relocation. This sign-on bonus will be subject to repayment to the Company if you voluntarily resign or are terminated by the Company for cause within one year of your relocation (to be further defined under "Relocation").
Target Bonus:	Your annual target bonus will be 40% of your base salary based upon the achievement of your individual goals, the achievement of team goals and the achievement of corporate goals. Your annual target bonus is subject to review and approval by the aTyr Board of Directors or Compensation Committee of the Board of Directors.

Equity:

As promptly as practicable after commencement of your employment with the Company, and subject to approval by the Board of Directors (or the Compensation Committee of the Board of Directors), you will be granted an option to purchase 153,000 shares of the Common Stock of the Company (the "Option") pursuant to the Company's 2015 Stock Option and Incentive Plan (the "aTyr Plan"). Subject to your continued full-time employment with the Company, the shares subject to the Option shall vest over a four (4) year period from your employment start date, with a one (1) year cliff, such that one-fourth (1/4) of the shares subject to the Option shall vest on the first year anniversary of your employment start date and the remainder of the shares shall thereafter vest in equal monthly installments over the subsequent three (3) years. The exercise price per share of the Option shall be determined based on the closing price of the Common Stock as reported on NASDAQ on the effective date of the grant. The specific terms and conditions of your Option will be subject to the terms of the aTyr Plan, as well as the terms set forth in a Stock Option Agreement between you and the Company.

In addition, subject to approval by the Board of Directors (or the Compensation Committee of the Board of Directors), you will be granted an option for 10,750 shares of Common Stock of the Company pursuant to the aTyr Plan (the "Trigger Option"). Subject to your continued employment with the Company, the shares subject to the Trigger Option will begin to vest upon the achievement of certain performance goals consistent with options previously granted to the Company's senior management team, which must be achieved within two years of the grant date. At that time, the four (4) year vesting schedule (the "Time-Based Vesting") will begin at a monthly rate. The specific terms and conditions of this option will be subject to the terms of the aTyr Plan, as well as terms set forth in the Stock Option Agreement between you and the Company.

Both the Option and the Time-Based Vesting with respect to the Trigger Option shall be subject to full acceleration in the event you are terminated by the Company without Cause or resign for Good Reason within two months prior to and twelve months following a Sale Event (as such capitalized terms are defined in the aTyr Plan).

Severance Policy: Subject to final approval by the Compensation Committee, you will be eligible for aTyr's Executive Severance Policy. This policy will include severance provisions for "Not for Cause" separations as well as "Change in Control" separations. The specifics of the plan will be provided to you.

Relocation: The Company shall reimburse you for the reasonable, out of pocket expenses that you incur in connection with relocating from New York to the San Diego area, up to a maximum amount of (i) $30,000 with respect to items that would not be included as taxable income and (ii) $96,000 (this amount includes gross-up tax costs) with respect to items that would be included as taxable income, with such amounts in clause (ii) to be paid in 2 lump sums, upon commencement of your employment with the Company and upon your relocation to the San Diego area. Any such reimbursement is subject to your submission of documentation sufficient to substantiate any such expenses and compliance with the Company's expense reimbursement policies and procedures. Notwithstanding the foregoing, no such reimbursement shall be payable later than the end of the calendar year after the calendar year in which you incurred the expense. In the event that your employment with the Company is terminated by the Company for cause or you voluntarily resign, in any event within one year after the date that you relocate, you shall no longer be eligible for any such reimbursements and you shall repay to the Company any relocation expenses previously reimbursed by the Company.

For purposes of this letter, your relocation shall be deemed complete on the date you provide the Company written confirmation of your new residence in the San Diego area.

Benefits: You will be entitled to receive standard medical, life and dental insurance benefits for yourself and your dependents in accordance with Company policy. Company reserves the right to change or eliminate these benefits on a prospective basis at any time.

401(k) Plan: You will be eligible to participate in the aTyr Pharma, Inc. 401(k) Savings Plan immediately following the start of your employment.

Vacation & Sick Time:	You will be entitled to accrue 15 days of vacation per year as a Full-Time employee. You will have 6 days of sick time available each year.
Holidays:	You will be eligible for aTyr's paid holidays. The schedule is published prior to the beginning of each calendar year.
Employment at Will:	Your employment will be at-will, which means it may be terminated at any time by you or the Company for any reason, with or without cause, and that your employment is not for any specific period of time. Any change to the at-will employment relationship must be by a specific, written agreement signed by you and the Company's Chief Executive Officer.
Start Date:	Monday, November 16, 2015 or a mutually agreed upon date.

As a condition of your employment, you will be required to sign and abide by our Employee Nondisclosure and Assignment Agreement (the "Employee NDA") when you begin your employment. A copy is attached for your reference. As a condition of your employment, you will also be required to abide by the Company's code of conduct and other policies applicable to employees as set forth in the Company's employee handbook in effect from time to time. A copy will be made available to you during your employment. In addition, in order to comply with the Immigration Reform and Control Act of 1986, within three (3) days of your Start Date you will be required to provide sufficient documentation to verify your identity and legal authorization to work in the United States. Please bring with you on your Start Date, the original of one of the documents noted in List A or one document from List B and one document from List C as itemized in the enclosed "Lists of Acceptable Documents". If you do not have the originals of any of these documents, please contact me immediately.

In the event of any dispute or claim relating to or arising out of your employment relationship with the Company, this agreement, or the termination of your employment with the Company for any reason (including, but not limited to, any claims of breach of contract, defamation, wrongful termination or age, sex, sexual orientation, race, color, national origin, ancestry, marital status, religious creed, physical or mental disability or medical condition or other discrimination, retaliation or harassment), you and the Company agree that all such disputes shall be fully resolved by confidential, binding arbitration conducted by a single arbitrator through the American Arbitration Association ("AAA") under the AAA's National Rules for the Resolution of

Employment Disputes then in effect, which are available online at the AAA's website at www.adr.org. The arbitrator shall permit adequate discovery and is empowered to award all remedies otherwise available in a court of competent jurisdiction and any judgment rendered by the arbitrator may be entered by any court of competent jurisdiction. By executing this letter, you and the Company are both waiving the right to a jury trial with respect to any such disputes. Company shall bear the costs of the arbitrator, forum and filing fees. Each party shall bear its own respective attorney fees and all other costs, unless otherwise provided by law and awarded by the arbitrator.

It is aTyr's policy to respect fully the rights of your previous employers in their proprietary or confidential information. No employee is expected to disclose, or is allowed to use for aTyr's purposes, any confidential or proprietary information he or she may have acquired as a result of previous employment.

I am pleased to extend this offer to you and look forward to your acceptance. Please sign and return the enclosed copy of this offer letter as soon as possible to indicate your agreement with the terms of this offer. This offer will lapse if not signed and returned by Sunday, October 25, 2015.

Once signed by you, this letter, together with the Employee NDA, will constitute the complete agreement between you and the Company regarding employment matters and will supersede all prior written or oral agreements or understandings on these matters.

Our mission is to discover life-changing therapies with relentless determination for people with grave maladies where others fall short. I believe you will be able to make an immediate contribution to this mission and I think you will enjoy the rewards of working for an innovative, fast-paced company. One of the keys to our success is top people. We hope you accept our offer to be one of those people.

Yours sincerely,

/s/John Mendlein
John Mendlein, Ph.D.
Executive Chairman and Chief Executive Officer

Enclosures

I accept the terms of employment as described in this offer letter dated October 23, 2015 and will start my employment on January 4, 2016. I confirm that by my start date at aTyr Pharma, Inc. I will be under no contract or agreement with any other entity which would in any way restrict my ability to work at aTyr Pharma, Inc. or perform the functions of my job for aTyr, including, but not limited to, any employment agreement and/or non-compete agreement.

/s/Sanuj Ravindran ***Date 11/22/2015***

Sanuj Ravindran, M.D.

aTyr Pharma, Inc.
3545 John Hopkins Court, Suite #250 San Diego CA 92121
Phone 858 731 8389 Fax 858 731 8394

Exhibit 10.19

March 30, 2016

Sanjay Shukla, M.D.

Re: Revised Offer of Employment

Dear Sanjay,

This letter is a formal offer setting forth the principal terms for you to join aTyr Pharma, Inc. ("aTyr" or the "Company"), a Delaware corporation, which is located in San Diego, California. This offer is contingent upon the satisfactory completion of references.

Position:	Chief Medical Officer
Location:	San Diego, CA
Status:	Full-Time, Exempt. This means you are paid for the job and not by the hour. Accordingly, you will not receive overtime pay if you work more than 8 hours in a work day or 40 hours in a workweek.
Reporting to:	John D. Mendlein, Ph.D., Executive Chairman and CEO
Base Salary Rate:	$15,625.00 semi-monthly (which equals $375,000.00 per year) less applicable withholdings, paid in accordance with Company's normal payroll practices during your Full-Time employment. Future adjustments in compensation, if any, will be made by the Company in its sole and absolute discretion.
Sign-On Bonus:	You will be offered a one-time sign-on bonus in the amount of $31,250.00 to be paid with your first paycheck. This sign-on bonus will be subject to repayment to the Company if you voluntarily resign or are terminated by the Company for cause within eighteen (18) months of your hire date.
Target Bonus:	Your annual target bonus will be 40% of your base salary based upon the achievement of your individual goals, the achievement of team goals and the achievement of corporate goals. Your annual target bonus is subject to review and approval by the aTyr Board of Directors or Compensation Committee of the Board of Directors. You must be employed by the Company at the time the bonus is paid in order to receive the bonus.

Equity:	As promptly as practicable after commencement of your employment with the Company, and subject to approval by the Board of Directors (or the Compensation Committee of the Board of Directors), you will be granted an option to purchase 163,000 shares of the Common Stock of the Company (the "Option") pursuant to the Company's 2015 Stock Option and Incentive Plan (the "aTyr Plan"). Subject to your continued full-time employment with the Company, the shares subject to the Option shall vest over a four (4) year period from your employment start date, with a one (1) year cliff, such that one-fourth (1/4) of the shares subject to the Option shall vest on the first year anniversary of your employment start date and the remainder of the shares shall thereafter vest in equal monthly installments over the subsequent three (3) years. The exercise price per share of the Option shall be determined based on the closing price of the Common Stock as reported on NASDAQ on the effective date of the grant. The specific terms and conditions of your Option will be subject to the terms of the aTyr Plan, as well as the terms set forth in a Stock Option Agreement between you and the Company.
Severance Policy:	Subject to final approval by the Compensation Committee, you will be eligible for aTyr's Executive Severance Policy. This policy will include severance provisions for "Not for Cause" separations as well as "Change in Control" separations. The specifics of the plan will be provided to you.
Benefits:	You will be entitled to receive standard medical, life and dental insurance benefits for yourself and your dependents in accordance with Company policy. Company reserves the right to change or eliminate these benefits on a prospective basis at any time.
401(k) Plan:	You will be eligible to participate in the aTyr Pharma, Inc. 401(k) Savings Plan immediately following the start of your employment.
Vacation & Sick Time:	You will be entitled to accrue 15 days of vacation per year as a Full-Time employee. You will have 6 days of sick time available each year.
Holidays:	You will be eligible for aTyr's paid holidays. The schedule is published prior to the beginning of each calendar year.

Employment at Will: Your employment will be at-will, which means it may be terminated at any time by you or the Company for any reason, with or without cause,and that your employment is not for any specific period of time. Any change to the at-will employment relationship must be by a specific, written agreement signed by you and the Company's Chief Executive Officer.

Start Date: Wednesday, March 30, 2016 or a mutually agreed upon date.

As a condition of your employment, you will be required to sign and abide by our Employee Nondisclosure and Assignment Agreement (the "Employee NDA") when you begin your employment. A copy is attached for your reference. As a condition of your employment, you will also be required to abide by the Company's code of conduct and other policies applicable to employees as set forth in the Company's employee handbook in effect from time to time. A copy will be made available to you during your employment. In addition, in order to comply with the Immigration Reform and Control Act of 1986, within three (3) days of your Start Date you will be required to provide sufficient documentation to verify your identity and legal authorization to work in the United States. Please bring with you on your Start Date, the original of one of the documents noted in List A or one document from List B and one document from List C as itemized in the enclosed "Lists of Acceptable Documents". If you do not have the originals of any of these documents, please contact me immediately.

In the event of any dispute or claim relating to or arising out of your employment relationship with the Company, this agreement, or the termination of your employment with the Company for any reason (including, but not limited to, any claims of breach of contract, defamation, wrongful termination or age, sex, sexual orientation, race, color, national origin, ancestry, marital status, religious creed, physical or mental disability or medical condition or other discrimination, retaliation or harassment), you and the Company agree that all such disputes shall be fully resolved by confidential, binding arbitration conducted by a single arbitrator through the American Arbitration Association ("AAA") under the AAA's National Rules for the Resolution of Employment Disputes then in effect, which are available online at the AAA's website at www.adr.org. The arbitrator shall permit adequate discovery and is empowered to award all remedies otherwise available in a court of competent jurisdiction and any judgment rendered by the arbitrator may be entered by any court of competent jurisdiction. By executing this letter, you and the Company are both waiving the right to a jury trial with respect to any such disputes. Company shall bear the costs of the arbitrator, forum and filing fees. Each party shall bear its own respective attorney fees and all other costs, unless otherwise provided by law and awarded by the arbitrator.

It is aTyr's policy to respect fully the rights of your previous employers in their proprietary or confidential information. No employee is expected to disclose, or is allowed to use for aTyr's purposes, any confidential or proprietary information he or she may have acquired as a result of previous employment.

I am pleased to extend this offer to you and look forward to your acceptance. Please sign and return the enclosed copy of this offer letter as soon as possible to indicate your agreement with the terms of this offer. This offer will lapse if not signed and returned by March 30, 2016.

Once signed by you, this letter, together with the Employee NDA, will constitute the complete agreement between you and the Company regarding employment matters and will supersede all prior written or oral agreements or understandings on these matters.

Our mission is to discover life-changing therapies with relentless determination for people with grave maladies where others fall short. I believe you will be able to make an immediate contribution to this mission and I think you will enjoy the rewards of working for an innovative, fast-paced company. One of the keys to our success is top people. We hope you accept our offer to be one of those people.

Yours sincerely,

/s/John Mendlein
John Mendlein, Ph.D.
Chief Executive Officer and Director

Enclosures

I accept the terms of employment as described in this offer letter dated March 30, 2016 and will start my employment on March 30, 2016. I confirm that by my start date at aTyr Pharma, Inc. I will be under no contract or agreement with any other entity which would in any way restrict my ability to work at aTyr Pharma, Inc. or perform the functions of my job for aTyr, including, but not limited to, any employment agreement and/or non-compete agreement.

/s/ Sanjay Shukla ***Date March 30, 2016***
Sanjay Shukla, M.D.

aTyr Pharma, Inc.
3545 John Hopkins Court, Suite #250 San Diego CA 92121
Phone 858 731 8389

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the following Registration Statements:

1. Registration Statement (Form S-3 No. 333-211998) of aTyr Pharma, Inc.,
2. Registration Statement (Form S-8 No. 333-203955) pertaining to ATYR PHARMA, INC. 2014 STOCK PLAN, ATYR PHARMA, INC. 2015 STOCK OPTION AND INCENTIVE PLAN, and the ATYR PHARMA, INC. 2015 EMPLOYEE STOCK PURCHASE PLAN, and
3. Registration Statement (Form S-8 No. 333-210543) pertaining to the ATYR PHARMA, INC. 2015 STOCK OPTION AND INCENTIVE PLAN, and the ATYR PHARMA, INC. 2015 EMPLOYEE STOCK PURCHASE PLAN;

of our report dated March 16, 2017, with respect to the consolidated financial statements of aTyr Pharma, Inc. included in this Annual Report (Form 10-K) for the year ended December 31, 2016.

/s/ Ernst & Young LLP

San Diego, California
March 16, 2017

Exhibit 31.1

CERTIFICATION OF PRINCIPAL EXECUTIVE OFFICER
PURSUANT TO RULE 13a-14(a) AND 15d-14(a) OF THE SECURITIES EXCHANGE ACT, AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, John D. Mendlein, certify that:

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

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

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

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

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

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

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

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

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

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

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

Date: March 16, 2017

/s/ John D. Mendlein
John D. Mendlein, Ph.D.
Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION OF THE PRINCIPAL FINANCIAL OFFICER
PURSUANT TO RULE 13a-14(a) AND 15d-14(a) OF THE SECURITIES EXCHANGE ACT, AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, John T. Blake, certify that:

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

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

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

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

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

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

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

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

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

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

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

Date: March 16, 2017

/s/ John T. Blake
John T. Blake
(Principal Financial and Accounting Officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350 AS ADOPTED PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of aTyr Pharma, Inc. (the "Company") for the period ended December 31, 2016, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, John D. Mendlein, Chief Executive Officer of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to my knowledge:

1. The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

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

Date: March 16, 2017

/s/ John D. Mendlein
John D. Mendlein, Ph.D.
Chief Executive Officer

The foregoing certification is being furnished solely to accompany the Report pursuant to 18 U.S.C. § 1350, and is not being filed for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, and is not to be incorporated by reference into any filing of the Company, whether made before or after the date hereof, regardless of any general incorporation language in such filing. A signed original of this written statement required by Section 906 has been provided to the Company and will be retained by the Company and furnished to the Securities and Exchange Commission or its staff upon request.

Exhibit 32.2

CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,AS ADOPTED PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002)

In connection with the Annual Report on Form 10-K of aTyr Pharma, Inc. (the "Company") for the period ended December 31, 2016, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, John T. Blake, Principal Financial and Accounting Officer of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to my knowledge:

1. The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

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

Date: March 16, 2017

/s/ John T. Blake
John T. Blake
Principal Financial and Accounting Officer

The foregoing certification is being furnished solely to accompany the Report pursuant to 18 U.S.C. § 1350, and is not being filed for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, and is not to be incorporated by reference into any filing of the Company, whether made before or after the date hereof, regardless of any general incorporation language in such filing. A signed original of this written statement required by Section 906 has been provided to the Company and will be retained by the Company and furnished to the Securities and Exchange Commission or its staff upon request.