

**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, 2017

or

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

For the transition period from _____ to _____

Commission file number: 001-37378

ATYR PHARMA, INC.

(Exact Name of Registrant as Specified in its Charter)

Delaware
(State or Other Jurisdiction of Incorporation
or Organization)

20-3435077
(I.R.S. Employer Identification No.)

3545 John Hopkins Court, Suite #250, San Diego, CA
(Address of Principal Executive Offices)

92121
(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, a smaller reporting company, or emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer Accelerated filer Non-accelerated filer Smaller reporting company Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

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 \$45,336,025 based on the closing price of the registrant's common stock on the Nasdaq Global Select Market of \$3.40 per share on June 30, 2017. 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 15, 2018 was 29,797,663.

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 2018 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, 2017.

ATYR PHARMA, INC.

ANNUAL REPORT ON FORM 10-K

For the Fiscal Year Ended December 31, 2017

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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 and Resolaris™. 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 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 our 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 our 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 our product candidates;
- the timing and success of the commercialization of our 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

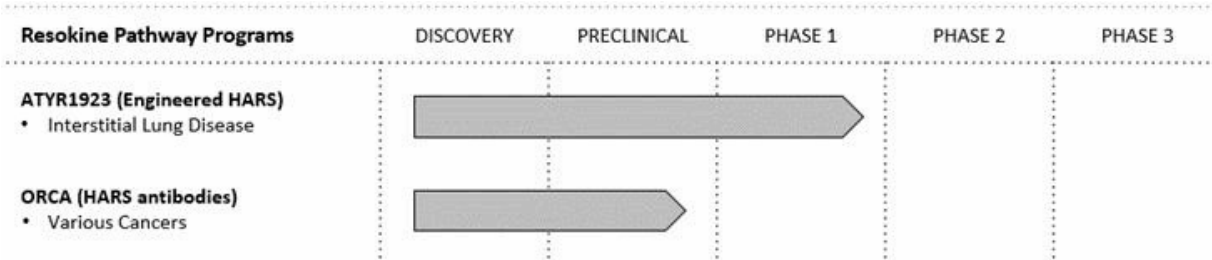
Item 1. Business

Overview

aTyr Pharma is a clinical-stage biotechnology company engaged in the discovery and clinical development of innovative medicines using its knowledge of tRNA synthetase biology. We have discovered novel extracellular functions of proteins derived from a number of tRNA synthetase genes, a family of more than 20 genes that influence immune function, and other activities, in previously unknown ways. Built on more than a decade of foundational science on extracellular tRNA synthetase biology and its effect on immune responses, we have built a global intellectual property estate directed to all 20 human tRNA synthetases as well as our product candidates.

Today, we focus on the therapeutic translation of the Resokine pathway, comprised of extracellular proteins derived from the histidyl tRNA synthetase (HARS) gene family, which has fueled a pipeline of novel drug candidate programs addressing disease areas of high unmet medical need, including cancer and lung disease. The pipeline below reflects those programs from the Resokine pathway that we are currently advancing.

Therapeutic Candidate Pipeline:



We embrace scientific transparency and commitment to research excellence as we chart drug targets from the Resokine family and other human tRNA synthetase genes that we hope will shape a better future of patient care.

Our intellectual property estate comprises of over 250 issued patents or allowed patent applications that are owned or exclusively licensed, including over 300 potential protein compositions derived from tRNA synthetase genes.

Strategy

Our mission is to translate our understanding of extracellular tRNA synthetase biology into novel first-in-class drug programs for conditions with unmet patient need.

Key elements of our strategy include the following:

Elucidate the therapeutic potential of proteins derived from tRNA synthetase genes, based on our leadership position in this new biology. Pathways emanating from tRNA synthetase gene families may represent an entire class of new drug targets. We are committed to translating these groundbreaking areas of newly discovered biology to therapeutic applications.

Build a diverse pipeline of biologics based on our understanding of extracellular tRNA synthetase biology. We continue to deepen our expertise in production of biologic product candidates and develop programs with multiple therapeutic modalities. Our initial programs have focused on agonizing or antagonizing the Resokine pathway and we are currently advancing two programs with potential applicability in cancer, lung disease, and other immune-mediated diseases.

Expand upon our knowledge and clinical experience with the Resokine pathway to address severe conditions characterized by immune imbalance. We seek to expand upon our knowledge and clinical experience with the Resokine pathway to address severe conditions characterized by immune imbalance. We believe that a protein therapeutic or antibody that modulates the threshold for T-cell activation without immunosuppression would have a unique and valuable competitive advantage across multiple disease settings.

Leverage our internal knowledge and exclusive worldwide rights to our product candidates to form meaningful collaborations to enhance our future development and commercial efforts. Our scientists are making discoveries internally and collaborating with academic research institutions to elucidate the potential functionality of extracellular proteins derived from human tRNA synthetase gene families. We aim to increase the breadth of these collaborations with both academic and industry partners to discover and develop drugs targeting additional pathways based on tRNA synthetase biology.

Our Science – tRNA Synthetase Biology

Extracellular tRNA synthetase biology represents a newly discovered set of potential physiological modulators and potential therapeutic intervention points.

Role of Ancient tRNA Synthetase Genes

tRNA synthetases were originally 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 many other researchers, have verified that tRNA synthetase gene products have a number of additional functional roles which may be mediated extracellularly by multiple splice variants from tRNA synthetase genes. Those functional roles include modulation of the immune system.

We are engaged in the discovery and development of innovative medicines using our knowledge of these newly discovered pathways in immunology effected by extracellular tRNA synthetases.

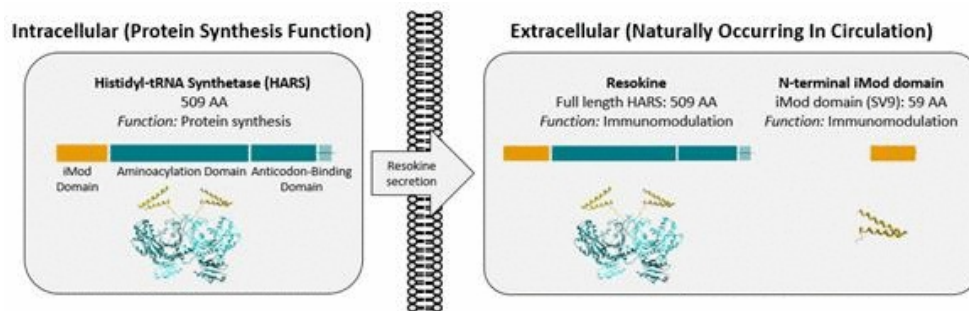
The Resokine Pathway – Modulating the Immune System

Overview of the Resokine Pathway

Our scientists were the first to discover the Resokine pathway, an extracellular pathway dependent upon a novel activity of the HARS protein and splice variants encoded by its gene.

The gene for HARS gives rise to a number of splice variants, many of which have lost their catalytic activity, but which retain the N-terminal domain of 59 amino acids. This domain was appended to HARS during evolution of multicellular organisms and is not essential for protein synthetic activity (as in prokaryotic organisms) but is retained with high homology across mammalian species. Proteins derived from the HARS gene, both full-length and splice variants, are present in human circulation and appear to play a role in modulating immune responses. We refer to the *extracellular* HARS proteins as Resokine, to differentiate them from the *intracellular* enzyme involved in protein synthesis.

The Resokine pathway is a prime example of a new discovery that may translate into new treatments. The importance of this newly-elucidated pathway is illustrated by the finding that antibodies to Resokine, generated in a rare human auto-immune condition, contribute to dysregulation of the immune system and disease.



Resokine is secreted from cells and circulates naturally in all individuals tested. The N-terminal domain (the immunomodulatory domain, or “iMod” domain) has structural similarity to a region of 4 alpha-helical bundle cytokines. Resokine has activity to modulate T-cell activation and importantly, the N-terminal iMod domain is conserved among all the characterized splice variants arising from the HARS gene.

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

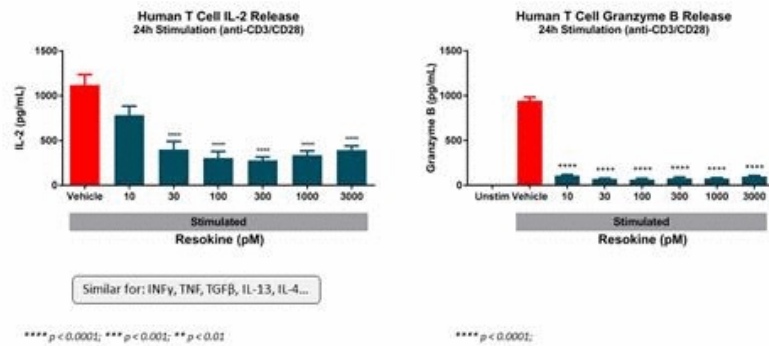
We conducted *in vivo* screening of the N-terminal iMod domain, which can be produced from a natural splice variant from the HARS gene, in several animal models of disease. In an acute rodent model administration of trinitrobenzene sulfonic acid, or TNBS, lead to severe immune cell activity or inflammation resulting in the death of the study animals. Animals administered the iMod domain survived significantly longer than those given either the vehicle control phosphate buffer solution, or an approved drug control (Budesonide) ($p < 0.01$), demonstrating the potential activity of the iMod domain as an immuno-modulator agent.

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. We believe our agonist programs harness the Resokine pathway and interact with T-cells to temper T-cell activation. In addition, we believe our antagonist program blocks this pathway thereby lowering the threshold for T-cell activation.

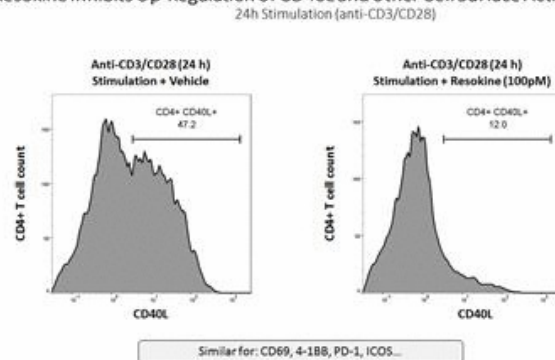
To test *in vitro* effects of Resokine on T cell activation, Resokine was tested by addition to T-cells undergoing activation *in vitro* with antibodies to CD3 and CD28. Resokine was able to significantly inhibit T-cell activation in these *in vitro* assays, as evidenced by a reduction of various cytokines, such as IL-2 and granzyme B, known to be markers related to T-cell activity.

Resokine Reduces Cytokine and Granzyme B Release during T Cell Activation



In vitro T-cell modulation experiments have demonstrated that at concentrations greater than 30 pM Resokine results in significant reduction of T-cell activation as shown by reduced expression of T-cell activation markers. Resokine appears to work to inhibit T-cell activation such that T-cells require enhanced stimulation to overcome the inhibitory effect.

Resokine Inhibits Up-Regulation of CD40L and other Cell Surface Activation Markers



Evidence of the Role of the Resokine Pathway in Patients

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 can develop a debilitating myopathy as well as severe interstitial lung disease, 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 most common form of anti-synthetase syndrome.

Based on these observations, we chose to study the potential link between HARS antibodies and 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 interstitial lung disease. 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.

Translation into Therapeutic Applications

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 Resokine may be used to modulate immune cell activity, especially in diseases wherein the pathophysiology of the disease may be driven by excessive T-cell activation. Our early clinical work increases our confidence that these proteins will continue to demonstrate a favorable safety and tolerability profile with no observed signs of general immunosuppression as we progress into later stage clinical trials.

Product Development Programs

Immuno-oncology

Overview of the ORCA Program

ORCA is a preclinical research program that targets the Resokine pathway using antibodies to bind to Resokine in tumor settings. We believe tumors, across multiple tumor types, may utilize Resokine to aid in the evasion of host anti-tumor immune responses. We have evaluated the therapeutic potential of targeting this novel pathway in multiple *in vitro* and *in vivo* tumor models, in comparison to and in combination with incumbent check-point modulators. Based on the tumor model data, we believe that targeting this pathway can reduce or, in some cases, reverse tumor growth either as a monotherapy or in combination therapy. ORCA represents a novel and proprietary target to block the Resokine pathway that we believe is active across multiple tumor types. Resokine is elevated across 100% of the tumor types tested and active in 95% or more of patients with a specific tumor type (15 types tested across over 450 patients).

In December 2017, we selected a panel of antibodies for continued preclinical development and initiated Chemistry, Manufacturing and Controls (CMC) activities for our ORCA program.

Extracellular Histidyl-tRNA Synthetase Gene Proteins With Immune Modulation Activity

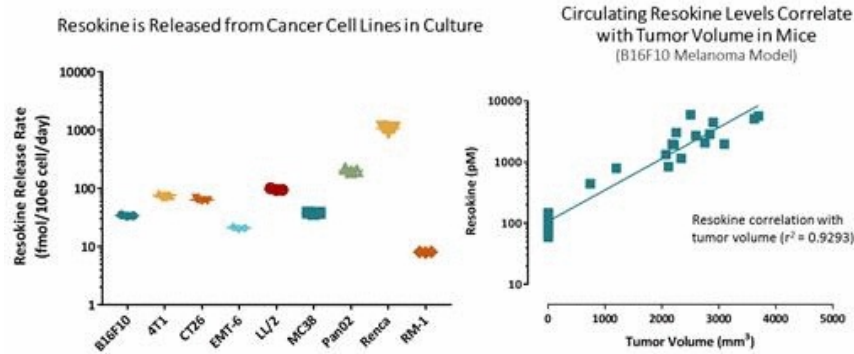
We refer to the extracellular proteins derived from the HARS gene as Resokine. Both the full-length and splice variants of Resokine are present in human circulation and play a role in modulating immune responses. Resokine proteins, all of which contain the N-terminal iMod domain, appear to have activity modulating T cell activity. We have conducted experiments to measure that the levels of iMod domain proteins are elevated in cancer, both in human plasma and in syngeneic tumor models in mice. In addition, monoclonal antibodies to the iMod domain appear to inhibit tumor growth in mice.

The N-terminal iMod domain is conserved among all the characterized splice variants arising from the HARS gene, and thus constitutes a potential epitope that can be targeted by antibodies to neutralize all forms of Resokine.

In combination with our knowledge of the agonist to the Resokine pathway and the experiments we have performed we believe these results demonstrate that Resokine has immunomodulatory activity *in vitro* through reduction in the extent of T cell activation. This activity appears to be dependent on the iMod domain because the recombinant iMod domain alone, or fused to immunoglobulin Fc (ATYR1923), has equivalent activity in these assays (data not shown). Resokine circulates naturally in all individuals tested, and appears to have immuno-modulatory activity, therefore we propose that Resokine may act as an “immune set-point” controlling the extent of T cell activation achieved with a given stimulus.

Resokine Levels are Elevated in Cancer

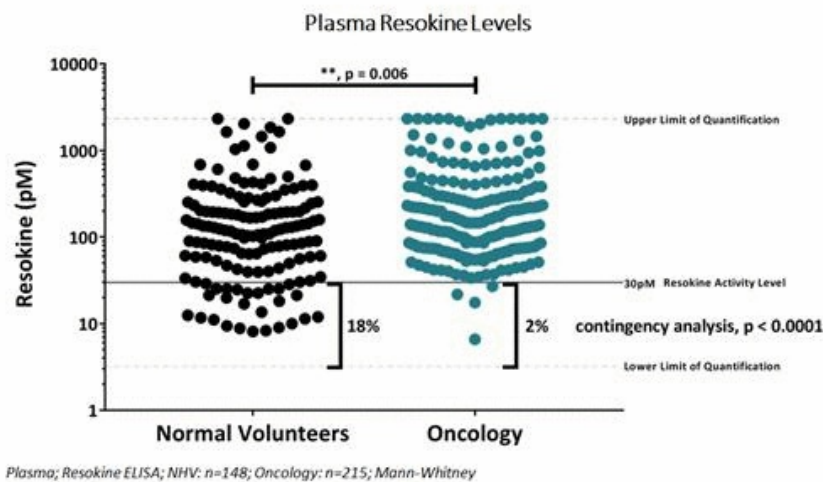
Resokine levels were measured from mouse or human samples using specific immunoassays with two non-competing antibodies to Resokine. Assays were carried out on the Meso Scale Discovery platform and verified using multiple formats.



In the experiments we conducted, we observed that Resokine appears to be released from cancer cell lines in culture. Levels vary from cell line to cell line.

Resokine levels in serum were significantly higher ($p < 0.001$) in B16F10 tumor-bearing mice as compared to normal mice. Resokine levels are increased in proportion to tumor growth, with levels increasing over 10-fold in very large B16F10 tumors.

Higher Plasma Resokine Levels Observed in Cancer Patients



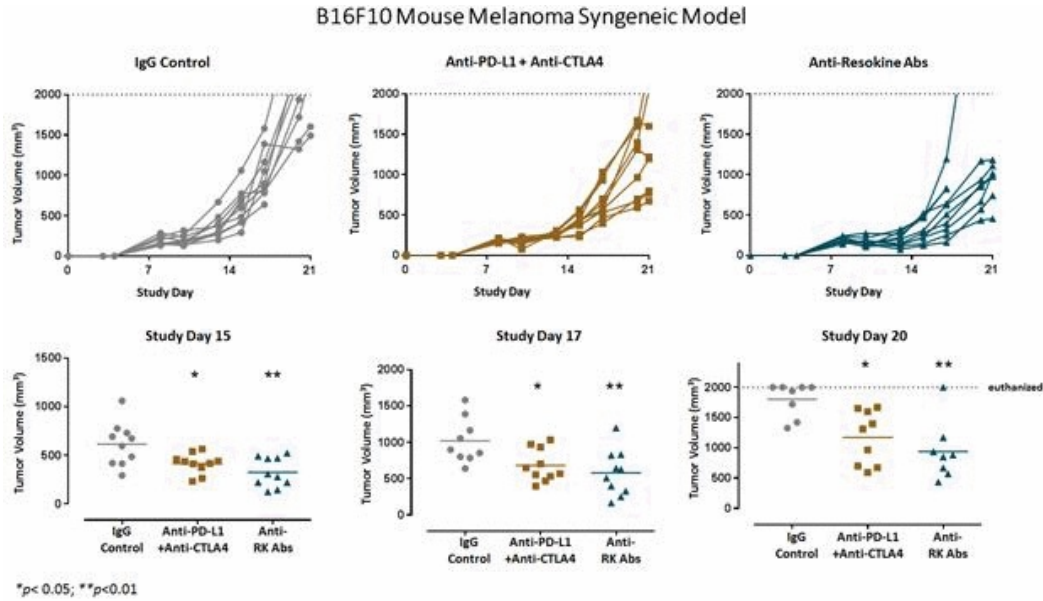
Human plasma samples from patients with tumors show a higher mean level of Resokine than normal healthy volunteers, and notably few patient samples have levels of Resokine below 30pM, a level with functional activity *in vitro*. Extended data sets show this pattern appears to be retained across multiple tumor types.

Resokine levels in healthy volunteers ($n = 148$) ranged from 8pM to > 2333pM with 18% of the individuals at a level below 30pM. In contrast, levels measured across patients ($n = 466$) with all tumor types tested ranged from 20pM to > 2333pM (above the upper limit of quantification) with only 4% of the patients at low levels, defined as < 30pM; ($p < 0.0001$).

We believe that Resokine secretion may be used by tumors as an additional mechanism to down-regulate anti-tumor immune responses. Since the levels of circulating Resokine are sufficient to modulate T cell activity, based on our *in vitro* experiments, we hypothesize that the enhanced release of Resokine from tumor cells may further increase the threshold stimulation required to generate an active immune response. There is the potential for this to be an additional mechanism by which tumor cells may evade immune responses.

Anti-Resokine Antibodies Have Anti-tumor Activity

We have evaluated the therapeutic potential of targeting this novel pathway in multiple *in vivo* tumor models, in comparison to and in combination with incumbent check-point modulators. Based on the tumor model data, we believe that targeting this pathway may reduce or, in some cases, reverse tumor growth either as a monotherapy or in combination therapy.

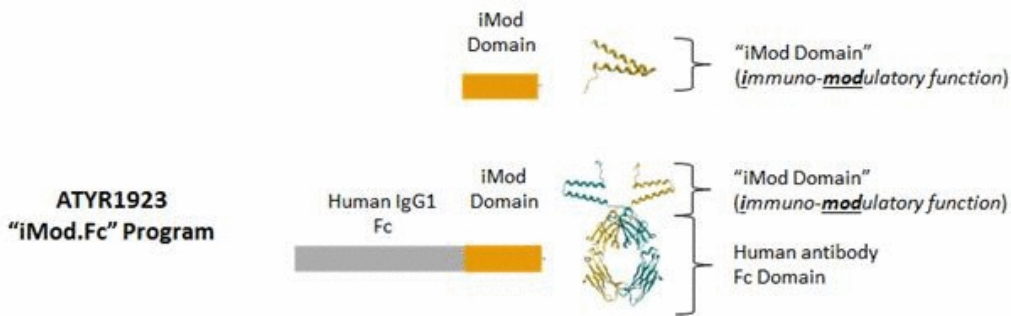


Anti-tumor activity was initially tested in the B16F10 syngeneic tumor model in C57Bl6 mice. B16F10 tumor cells (1x10⁴ cells in 0.1mL PBS/20% matrigel) were implanted subcutaneously on the right flank on day 0. Antibody therapy was administered by intraperitoneal injection on days -1, 6, and 13 (200 microgram/antibody/mouse). Tumor volumes were measured at indicated intervals over 21 days. Statistics are 1-way ANOVA, followed by Dunnett’s.

Immune-mediated Diseases

Overview of ATYR1923 (iMod.Fc Program)

We established the iMod.Fc program to leverage our knowledge of the Resokine pathway to vary exposure and activity of the iMod domain through protein engineering. The goal of the program was to develop a potential therapeutic which would possess only the N-terminal immuno-modulatory activities of Resokine and fuse it to the FC region of a human antibody.



Our Fc fusion experiments helped delineate how to increase the serum half-life and enhance the exposure of the iMod domain of Resokine while maintaining activity and provide insights into this domain harboring immuno-modulatory activity. Experiments have indicated that Fc fusion proteins can be generated which increase exposure and maintain iMod domain activity.

Interstitial Lung Diseases (ILDs) and the Role of Immunology

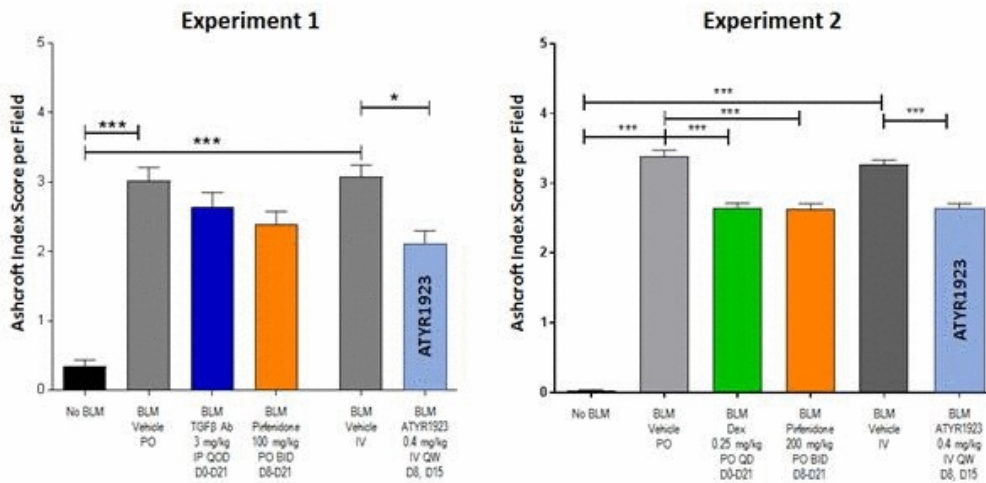
ILD develops in approximately 85% of Jo-1 positive anti-synthetase patients with antibodies to Resokine. It can include the presence of focal immune cell infiltrates and an acinar pattern of involvement on chest computed tomography (CT) scan, lymphocytic predominance on broncho-alveolar lavage and lymphocytic 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.

Among the various 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 ATYR1923 preclinical activities. Examples of pulmonary diseases with an immune component include idiopathic interstitial pneumonias, sarcoidosis, chronic hypersensitivity pneumonitis, idiopathic pulmonary fibrosis, and ILD in the setting of systemic sclerosis or rheumatoid arthritis.

Preclinical Development

To test our hypothesis that augmenting the Resokine pathway with ATYR1923 has therapeutic potential in ILD, we have generated data in a mouse model of lung inflammation and pulmonary fibrosis. ATYR1923 has also shown promising therapeutic activity in this bleomycin-induced model (as set forth in the figure below) which has been used as translational rationale 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.

ATYR1923 Ameliorates Fibrosis in Bleomycin-Induced Lung Injury



PO = oral dosing; IV = intravenous dosing; BLM = Bleomycin; Dex = Dexamethasone

ATYR1923 administered therapeutically drives activity comparable to or greater than Pirfenidone, anti-TGF antibodies, and dexamethasone.

Experiment 1: Lung tissues collected on Day 21 (i.e., after 2 weeks of protein treatment) were stained with Masson's Trichrome stain. Ashcroft scores were assigned to 8-10 fields per animal; all analyzed fields are represented. Bleomycin induced an increase in histological fibrosis. ATYR1923 (0.4 mg/kg once weekly) significantly ameliorated fibrosis as measured by histological Ashcroft scoring. TGFβ blockade and pirfenidone did not have significant effects on fibrosis in this experiment (* $p < 0.05$; *** $p < 0.001$ vs. Vehicle IV, Kruskal-Wallis ANOVA followed by Tukey's post hoc test).

Experiment 2: Lung tissues collected on Day 21 (i.e., after 2 weeks of protein treatment) were stained with Masson's Trichrome stain. Ashcroft scores were assigned to 20 fields per animal; all analyzed fields are represented. Bleomycin induced an increase in histological fibrosis. ATYR1923 (0.4 mg/kg once weekly) significantly ameliorated fibrosis as measured by histological Ashcroft scoring (*** $p < 0.001$ vs. Respective Vehicle, Kruskal-Wallis ANOVA followed by Tukey's post hoc test).

These preclinical experiments were presented in a poster at the American Thoracic Society International Congress in Washington D.C. in May 2017.

Clinical Development Plan

We are conducting a first-in-human Phase 1 clinical trial of ATYR1923. This randomized, double-blind, placebo-controlled study will investigate the safety, tolerability, immunogenicity, and pharmacokinetics of intravenous ATYR1923 in healthy volunteers. The study will enroll 36 subjects into one of six sequential cohorts and subjects will be randomized 2:1 to receive a single infusion of ATYR1923 or placebo. Ascending ATYR1923 doses by cohort range from 0.03 mg/kg to 5.0 mg/kg.

We anticipate learning more about the safety profile and tolerability of ATYR1923 as well as some characteristics of its pharmacokinetics and dosing potential. In parallel, we are expanding our knowledge of the therapeutic potential of ATYR1923 by conducting several *in vivo* and *in vitro* models to further elucidate its potential clinical utility. These data, as well as the Phase 1 clinical trial results, will help inform selection of the indication for future clinical trials for our ATYR1923 program.

Overview of ATYR1940 (Resolaris)

We internally discovered and developed ATYR1940, our first therapeutic candidate based on a protein naturally secreted from muscle (Resokine) that may act to influence T-cell activation at the tissue level to promote healthier muscle. There is potential that ATYR1940 may translate into an innovative therapeutic for rare genetic myopathies with an immune component, including limb-girdle muscular dystrophy (LGMD), facioscapulohumeral muscular dystrophy (FSHD), and Duchenne muscular dystrophy (DMD). We collected evidence that supports applicability of ATYR1940 as an example of adding back a protein that is insufficiently produced by the human body to potentially counteract disease.

Current Status

At this time, we are not pursuing additional clinical development of ATYR1940 without a significant collaboration or strategic partnership. This decision is based on prioritizing the other programs in the pipeline, which we feel have an opportunity to add significant value and support translation of our science into the clinic in a more capital efficient manner.

Safety and Tolerability Profile

ATYR1940 is a slightly truncated version of the full Resokine protein. As such, the early clinical safety and tolerability data has high utility for all our Resokine pathway based programs.

Our early clinical development for ATYR1940 evaluated three rare genetic myopathies: adult FSHD, early onset FSHD, and LGMD2B where there is no therapeutic standard of care currently available. This allowed us to collect important information related to the safety, tolerability and immunogenicity of our first product candidate 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 for all our programs related to the Resokine pathway.

To date, 44 patients have received ATYR1940 across three 3-month clinical trials with two extension studies for a total drug exposure of 204 patient months. In those trials, ATYR1940 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 was 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 was 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.

Our Discovery Engine for Therapeutic Applications of tRNA Synthetase Biology

We plan to leverage our discovery engine to identify other tRNA synthetase pathways of interest and select additional product candidates for preclinical and clinical investigation in a variety of disease settings through a combination of efforts between ourselves, Pangu Biopharma Ltd., our subsidiary, and the Scripps Research Institute.

We believe our strategy of understanding extracellular tRNA synthetase function by using *in vivo* experiments early and often while using patient data to focus this *in vivo* exploration has been validated by our early-stage clinical programs. Additionally, we believe our discovery engine can be applied to other members of the tRNA synthetase family to help identify additional clinical utility.

We believe this new biology presents novel protein therapeutic development opportunities based on the modulation of important immunological pathways applicable to multiple diseases. In addition to our own internal development work, we will work with collaborators and academia to further understand the potential clinical utility and mechanism of tRNA synthetase biology.

Collaborations

The Scripps Research Institute

We are party to an amended and restated research funding and option agreement with The Scripps Research Institute, or TSRI, specifically for the laboratory of our Board Member and founder Dr. Paul Schimmel. Under the agreement, we provide funding to TSRI to conduct certain research activities related to aminoacyl tRNA synthetases. The agreement renews automatically for \$0.7 million in 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. As of May 31, 2018, we will have provided \$2.0 million of funding for the preceding 12-month period. 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 tRNA synthetase biology. In December 2017, 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 2018 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.

Competition

The biotechnology and pharmaceutical industries are intensely competitive. We will face competition with respect to our product candidates and any other therapeutics we may develop or commercialize in the future, from pharmaceutical companies, biotechnology companies, universities and other research institutions. Our competitors may have substantially greater financial, technical and other resources, such as larger research and development staff and established 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 novel functions of tRNA synthetases we are aware of other companies that are developing products that could compete as treatments for our targeted indications, as described below.

ORCA Program

There are a number of companies engaged in the development of immunotherapies to be used alone, or in combination, to treat various oncology indications across a range of tumor types. While we are not aware of any other companies developing antibodies to Resokine as a target for immunotherapy, the immuno-oncology field is competitive, with treatments currently approved and on the market or in development with various mechanisms of action, targeting various tumor types and patient populations from a variety of different companies including Merck & Co., Inc., Bristol Myers Squibb, Roche, AstraZeneca, Pfizer and Merck KGaA, all of which have significantly greater resources than we do. Our program, if successful, will likely face significant competition both by therapeutics that are already being marketed as well as those that will be approved for marketing before our program.

ATYR1923

We are aware of three FDA approved products with indications for the treatment of specific forms of ILD. Esbriet® (pirfenidone), marketed globally by F. Hoffmann-La Roche AG, Shionogi Ltd. and Il Dong Pharmaceutical, and Ofev® (nintedanib), a small molecule tyrosine-kinase inhibitor marketed globally by Boehringer Ingelheim, both were approved in October 2014 to treat Idiopathic Pulmonary Fibrosis (IPF). H.P. Acthar Gel (repository corticotropin injection) is marketed globally by Mallinckrodt plc for a number of indications, including symptomatic sarcoidosis. There are a number of companies engaged in the clinical development of potential new therapeutics for various forms of ILD, including Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, FibroGen, Inc., Galapagos NV, Kadmon Holdings, Inc., GlaxoSmithKline, and Roche.

ATYR1940

There are currently no FDA approved therapeutics for the treatment of FSHD or LGMD2B. 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. Myonexus is developing MYO-201 for the treatment of LGMD2B. This gene therapy approach is currently in a FDA-required intramuscular Phase 1 study to assess safety.

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.

Additional capabilities important to the marketing of therapeutics 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.

ORCA Program

ORCA is a preclinical immuno-oncology research program that targets the Resokine pathway using antibodies to bind to Resokine in tumor settings. We are currently in early stages of CMC activities, including cell line development contracted at a CRO and have selected a CDMO for GMP manufacturing.

ATYR1923

ATYR1923 is a Fc fusion molecule that is expressed in recombinant *E.coli* by expression in inclusion bodies and refolding to recreate the native structure. We have worked with CDMOs in the United States on the development and GMP manufacturing process for the successful production of ATYR1923 preclinical and clinical drug substance and drug product for initial Phase 1/2 studies. We contract with CROs to conduct labeling, storage and distribution of ATYR1923 to clinical sites.

ATYR1940

ATYR1940 is expressed in recombinant *E.coli*, purified, formulated, filled and packaged for clinical use. For our Phase 1b/2 clinical trials conducted to date, the drug substance for ATYR1940 was manufactured by a CDMO in India. ATYR1940 drug product for such Phase 1b/2 clinical trials was manufactured by CDMOs in India and the United States.

We are working with a CDMO in the United States, and have completed the development, scale-up and GMP manufacturing process for the production of ATYR1940 drug substance to meet the needs of any future clinical development. We have also successfully demonstrated comparability of the product manufactured with the different process and scales and at different sites. The drug product process for ATYR1940 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 ATYR1940 drug product 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 extracellular tRNA synthetase biology.

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.

ORCA Program

Our ORCA patent portfolio is comprised of a number of patent families related to antibodies to novel epitopes and specific HARS splice variants, methods of use claims for the treatment of cancer, vaccines and methods of vaccination, and therapeutic compositions to human and humanized antibodies to HARS. These applications have been filed in the United States as U.S. provisional applications and in some cases as international applications under the Patent Cooperation Treaty, or PCT, or in some cases as continuations of existing previously filed cases. If issued, these patents are predicted to expire between 2030 and 2037, absent any patent term extensions.

ATYR1923

Our ATYR1923 patent portfolio is comprised of a number of patent families related to derivatives of Resokine, including the iMod domain, related splice variants, combinations with other therapeutics, and next-generation product forms with modified therapeutic activity or pharmacokinetic characteristics. As of February 8, 2018, our ATYR1923 patent portfolio includes a patent family that is jointly owned by us and our 98% owned subsidiary, Pangu Biopharma, and includes three issued U.S. patents, two patents issued in Japan, and one in each of Europe, China, and Australia, and patent applications pending in the United States, Canada, Europe, China, Japan, and Hong Kong. The U.S. patents are expected to expire between 2030 and 2031, absent any patent term extension for regulatory delays, and the ex-U.S. patents, and patents that issue from these patent applications, if any, are expected to expire in 2030, absent any patent term extension. The ATYR1923 patent portfolio also includes another patent family jointly owned by us and Pangu Biopharma, which includes patent applications directed to related splice variants of HARS. This patent family includes two issued US Patents, and one patent issued in each of Europe, Japan, China, Australia, and New Zealand. Patent applications are pending in the United States, India, Japan, Korea, Russia and Hong Kong. Patents that issue from these patent applications, if any, are expected to expire in 2031, absent any patent term extension. Also included within the ATYR1923 patent portfolio are pending patent applications directed to specific product forms of ATYR1923, ATYR1940, and other HARS splice variants, and patent families directed to Fc fusion proteins, and combinations for treating lung inflammation. These applications have been filed in the United States as U.S. provisional applications and in some cases as international applications under the PCT. If issued, these patents are predicted to expire between 2033 and 2038, absent any patent term extensions.

ATYR1940

Our ATYR1940 patent portfolio is comprised of a number of patent families directed to ATYR1940 and related proteins. As of February 8, 2018 our ATYR1940 patent portfolio includes a patent family that is jointly owned by us and our 98% owned subsidiary, Pangu Biopharma, and includes two issued U.S. patents, and one patent issued in each of Australia, Europe, Japan, and South Africa and New Zealand and patent applications pending in the United States, Brazil, Canada, China, India, Korea, Mexico, New Zealand, and Russia. The U.S. patents and patents that issue from these patent applications, if any, are expected to expire in 2033, absent any patent term extension for regulatory delays. Our ATYR1940 patent portfolio also includes a second patent family that is wholly owned by us and that includes patents and pending patent applications that are directed to ATYR1940 and related proteins. This second patent family includes three issued U.S. patents and patents issued in Europe, Japan, China, and Australia, and Hong Kong as well as related patent applications that are pending in the United States, Australia, Canada, Europe, China, and Japan. The U.S. patents are expected to expire in 2030 and 2031, absent any patent term extension for regulatory delays, and the ex-U.S. patents, and patents that issue from these applications, if any, are expected to expire in 2030, absent any patent term extension. Also included with the ATYR1940 patent portfolio are pending patent applications directed to specific methods of use of ATYR1940 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 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. Patents that issued from these applications, if any, are predicted to expire between 2033 and 2037, absent any patent term extensions.

Our pipeline of extracellular tRNA synthetase proteins is covered by a series of 21 patent families, which are directed to all 20 human cytosolic tRNA synthetases. At least 42 patents are issued in the United States, including patents directed to specific therapeutic protein compositions, the corresponding protein polynucleotide sequences, and applications directed to antibody compositions to specific splice variants. 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.

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 IND submission includes 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, and the sponsor of an approved BLA or NDA is also subject to an annual prescription drug product program fee. These fees are typically increased annually. Applications for orphan drug products are exempted from the BLA and NDA 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. 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.

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, 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 or some changes to the manufacturing process, are subject to prior FDA review and approval.

Drug manufacturers are subject to periodic unannounced inspections by the FDA and state agencies for compliance with cGMP requirements.

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, or result in the imposition of post-market studies or trials to assess new safety risks.

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.

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. 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

There is an abbreviated approval pathway for biological products shown to be biosimilar to, or interchangeable with, an FDA-licensed reference biological product. 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.

Abbreviated New Drug Applications for Generic Drugs

To obtain approval of a generic drug, an applicant must submit an abbreviated new drug application, or ANDA, to the FDA. 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.

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.

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 medicinal product 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 medicinal product 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 medicinal product 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 medicinal product 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 medicinal product 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.

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. For example, the Bipartisan Budget Act of 2018, or the BBA, among other things, amends the Affordable Care Act, effective January 1, 2019, to reduce the coverage gap in most Medicare Part D plans, commonly referred to as the "donut hole." The BBA also extended the coverage gap discount program to include biosimilars starting in 2019. The Tax Cuts and Jobs Act of 2017 includes a provision repealing, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate." On January 22, 2018, President Trump signed a continuing resolution on appropriations for fiscal year 2018 that delayed the implementation of certain ACA-mandated fees, including the so-called "Cadillac" tax on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain high cost employer-sponsored insurance plans, the annual fee imposed on certain health insurance providers based on market share, and the medical device excise tax on non-exempt medical devices. Further, 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 modify, repeal, or 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 15, 2018 we had 65 full-time and part-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 \$1.07 billion or more; (ii) December 31, 2020; (iii) the date on which we have issued more than \$1.0 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 our financial condition and need for additional capital

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 \$48.2 million, \$57.9 million, and \$48.0 million for the years ended December 31, 2017, 2016 and 2015, respectively. As of December 31, 2017, we had an accumulated deficit of \$264.2 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 venture debt and term loans. 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.

We expect to continue to incur significant expenses and operating losses for the foreseeable future. We anticipate that our expenses will fluctuate in connection with our ongoing activities as we: continue our research and preclinical and clinical development of product candidates from our ORCA program, ATYR1923 or any other product candidates that we may develop; further develop the manufacturing process for our product candidates; seek regulatory approvals for our product candidates that successfully complete clinical trials; ultimately 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; maintain, protect and expand our intellectual property portfolio; acquire or in-license other product candidates and technologies; attract and retain skilled personnel; and create additional infrastructure to support our operations as a public company and our product development and planned future commercialization efforts.

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 our product candidates. 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 our product candidates, potentially with a strategic 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 our product candidates and establish supply and manufacturing relationships with third parties;
- 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 intellectual property portfolio;
- obtaining market acceptance of tRNA synthetase-based therapeutics and our product candidates as viable treatment options for our target indications;

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

Even if one of our product candidates is approved for commercial sale, we anticipate incurring significant costs associated with commercializing any such 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. 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 need to raise additional capital or enter into strategic partnering relationships to fund our operations.

We are currently advancing two therapeutic programs in different therapeutic areas. The development of therapeutic product candidates is expensive, and we expect our research and development expenses to increase.

As of December 31, 2017, our cash, cash equivalents and available-for-sale investments were approximately \$85.1 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 offerings 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 number and characteristics of product candidates that we pursue;
- 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 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.

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.

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. 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.

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. For example, we have decided not to pursue additional clinical development of ATYR1940 without a significant collaboration or strategic partnership for this program. 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 ATYR1940 or any of our other 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.

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

In November 2016, we entered into a loan and security agreement, or Loan Agreement, for a term loan with Silicon Valley Bank and Solar Capital Ltd., to borrow up to \$20.0 million principal in new term loans, \$10.0 million of which was funded in November 2016, \$5.0 million of which was funded in June 2017 and \$5.0 million of which was funded in December 2017. The Term Loans are 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.

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 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 Loan Agreement includes a material adverse change clause, which enables the Lenders to require immediate repayment of the outstanding debt. The material adverse change clause covers a material impairment in the perfection or priority of the lenders' lien in the underlying collateral or in the value of such collateral, material adverse change in business operations or condition or material impairment of our prospects for repayment of any portion of the remaining debt obligation.

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 Loans to become immediately due and payable.

Risks related to the discovery, development and regulation of our product candidates based on tRNA synthetase biology

Our current product candidates 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 extracellular functions of tRNA synthetase biology, a newly discovered area of biology. Our future success is highly dependent on the successful development of product candidates based on tRNA synthetase biology, including our current product candidates and additional product candidates arising from the Resokine pathway or other pathways. Extracellular tRNA synthetase-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, proteins and related antibodies from the Resokine pathway and from other tRNA synthetase pathways 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 tRNA synthetases 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 therapeutic product candidates 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 therapeutic product candidates that are safe, effective, approvable by regulatory authorities, manufacturable, scalable, or profitable.

Because our work in tRNA synthetase 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 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 extracellular tRNA synthetase-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 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 therapeutic candidates 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.

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 our product candidates 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. Our knowledge of the activity of this pathway in Jo-1 antibody patients may not be applicable to our target patient populations. In addition, our classification of diseases based on the existence of excessive immune cell activation or lack thereof and

our hypothesis that these represent potential indications for our product candidates 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 our product candidates will adversely affect 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 our therapeutic product candidates 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 product candidates related to the Resokine pathway, including conducting preclinical studies and clinical trials. We have not yet commenced or completed any evaluation of our product candidates in human clinical trials designed to demonstrate efficacy to the satisfaction of the FDA. Before we can market or sell our therapeutic candidates 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 our therapeutic candidates. If we do not receive regulatory approvals for our product candidates, 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 our therapeutic candidates, 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.

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 any clinical trials that we are conducting or may plan to conduct, will be initiated or conducted as planned or completed on schedule, if at all. For example, following our submission of an investigational new drug application, or IND, to the FDA to evaluate ATYR1940 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 issue of the comparability of the drug substance used in our preclinical toxicology studies to that previously used with that proposed for use in the U.S. clinical trial. After we submitted our response, in January 2015, FDA removed our IND 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 ATYR1940 at doses higher than 3.0 mg/kg. The FDA lifted the partial clinical hold 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 our 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 (as we did with ATYR1940 with 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.

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 tRNA synthetase-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.

Our therapeutic product candidates 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 our product candidates, 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 for ATYR1940, we observed low levels of antibodies to ATYR1940 in some subjects in response to the administration of ATYR1940. 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 ATYR1940 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. Some patients in our Phase 1b/2 clinical trials of ATYR1940 experienced generalized infusion related reactions, or IRRs, and discontinued dosing. We established procedural measures, including a decreased concentration and intravenous delivery rate of ATYR1940, 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 be effective in minimizing the occurrence of generalized IRRs or the formation of anti-drug antibodies in any future clinical trials, or result in the retention of patients in future clinical trials. Generalized IRRs and other complications or side effects could harm further development and/or commercialization of our 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 our product candidates. 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.

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 extracellular proteins derived from tRNA synthetases (or antibodies targeting tRNA synthetase biology) to develop product candidates 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 diseases. Our research programs may initially show promise in identifying potential product candidates, 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 product candidates 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 certain of 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 clinical trials for our product candidates is critical to our success. Certain of the conditions for which we may elect to evaluate our product candidates may be rare diseases with limited patient pools from which to draw for clinical trials. 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 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 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 tRNA synthetase-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. 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 our tRNA synthetase-based therapeutic candidates 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. For example, we changed cell lines for the production of ATYR1940 in connection with the engagement of a new CDMO 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 tRNA synthetases represent a class of proteins that may share immunomodulatory properties in various physiological pathways, each tRNA synthetase 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 ATYR1923, 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 tRNA synthetase-based therapeutic candidates. Currently, we are producing our ATYR1923 molecule in *E.coli* by expression in inclusion bodies and refolding to recreate the native structure. With regard to our ORCA program we are working with third parties for cell line development and antibody manufacturing which may be subject to delays or staging based on our program priorities or other third party factors that may be beyond our control. 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 clinical trials or on a commercial scale will harm our business, prospects, financial condition and results of operations.

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.

Although the FDA and the European Commission have granted orphan drug designation to ATYR1940 for the treatment of FSHD and LGMD, we may not receive orphan drug designation for ATYR1940 in other jurisdictions or for other indications that we may pursue, or for any other of our product candidates 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 ATYR1940 for the treatment of FSHD and for the treatment of LGMD. We may also apply for orphan drug designation for other product candidates and for ATYR1940, if we are able to engage a collaborative or strategic partner for further development, in other territories and for other indications. 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.

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 ATYR1940 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 our other product candidates, although we may elect not to do so. A breakthrough therapy designation 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 designation 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 ATYR1940 for the treatment of FSHD and LGMD2B, or even if we receive breakthrough therapy or fast track designation for 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 we obtain regulatory approval for a product candidate, such product will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping, conduct of post-marketing studies, adverse event reporting 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.

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. 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. 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, agreements that would materially restrict the manner in which we promote or distribute our drug products and exclusion from Medicare, Medicaid and other federal and state healthcare programs. 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. 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.

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 any 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 GCPs 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 and intend to rely on third parties to produce nonclinical, clinical and commercial supplies of our product candidates.

Other than some internal capacity to support pre-clinical activities, 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.

With regard to our ORCA program, we are currently in early stages of CMC activities, including cell line development contracted at a CRO and have selected a CDMO for GMP manufacturing. We currently rely on a single CDMO for process development and scale-up of ATYR1923, including the manufacture of bulk drug substance for our projected needs for initial clinical trials. We relied on a single CDMO for bulk drug substance for ATYR1940 for our projected needs for anticipated pivotal clinical trials. If we pursue further development of ATYR1940 with a collaboration or strategic partnership, subject to the satisfactory completion of process validation and other requirements, we may contract with this CDMO for larger scale commercial manufacturing. 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 based on tRNA synthetase biology. 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 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.

Patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time.

Patents have a limited lifespan. In the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired, we may be open to competition from competitive products, including generics or biosimilars. Given the amount of time required for the

development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours.

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

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 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 recently experienced a leadership transition. On November 1, 2017, Sanjay S. Shukla, M.D., M.S., our Chief Medical Officer, succeeded John D. Mendlein, Ph.D., our prior Chief Executive Officer. Dr. Shukla is now serving as our President and Chief Executive Officer. Our future performance will depend, in part, on our ability to successfully transition Dr. Shukla to his new role, continue to retain and attract senior management talent, including qualified medical expertise and leadership to supplement the executive team. Our failure to manage this transition effectively could result in inefficiencies in the development and commercialization of our product candidates, timing and outcomes of future regulatory approvals, advancement of our business development efforts and results of operations.

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 have conducted clinical trials in the European Union and in Australia and may conduct future clinical trials internationally. 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.

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, financial condition and results of operations.

We have incurred and will continue to incur significant 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 have incurred and will continue to incur 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. For example, the global financial crisis caused extreme volatility and disruptions in the capital and credit markets. For example, in March 2017, the U.K. government provided official legal notification to the European Union that the U.K. will exit 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 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 conduct our Phase I clinical trial for ATYR1923 in Australia and sponsor research in Hong Kong. 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 CDMOs, 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 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.

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 our product candidates, 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 any of our product candidates. Although we intend to rely on third-party manufacturers for commercialization, 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 our product candidates, 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, our product candidates, 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.

The biotechnology and pharmaceutical industries are intensely competitive and subject to rapid and significant technological change. We have competitors both in the United States and internationally, including major multi-national pharmaceutical companies, biotechnology companies and universities and other research institutions. 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.

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.

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.

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.

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 15, 2018, based on the latest information available to us, our executive officers, directors, principal stockholders and their affiliates beneficially own approximately 78.5% of our voting stock, including 14.8% held by entities affiliated with EcoR1 Capital and 9.50% held by Viking Global Opportunities Illiquid Investments Sub-Master LP (VGO Fund, together with its affiliates, Viking). The percentage of our common stock beneficially owned by Viking would increase substantially if Viking waived the ownership percentage limitation of 9.50% of the shares of our common stock then issued and outstanding (Viking Percentage Limitation) and would further increase substantially if we obtained the approval of our stockholders to the extent required in accordance with the NASDAQ Global Market rules (the Requisite Approval) (up to 38.5% assuming no other shares of common stock were issued upon exercise of the warrants purchased by all other selling stockholders). VGO Fund can waive or change the Viking Percentage Limitation on 61 days notice. Assuming all of the shares issued in the Private Placement are sold by the purchasers in such transaction, our executive officers, directors, principal stockholders and their affiliates would beneficially own approximately 25.4% of our voting stock. Therefore, our executive officers, directors, principal stockholders and their affiliates 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 \$1.07 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 \$1.07 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 addition, sales of a substantial number of shares of our common stock by our existing stockholders (including those stockholders who purchased securities in our Private Placement) 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. For example, we registered 5,740,048 shares of our common stock, 11,429,760 shares of our common stock issuable upon the conversion of an aggregate of 2,285,952 shares of Class X Convertible Preferred Stock and 6,438,678 shares of our common stock issuable upon exercise of warrants issued by us in the Private Placement for resale on a Form S-3, which was declared effective by the SEC on September 27, 2017. As a result, the common stock is currently available for resale to the public and to the extent warrants are exercised by the holders and the Class X Preferred Stock is converted to common stock after obtaining stockholder approval and other conditions specified in the Securities Purchase Agreement, any shares of such common stock may result in dilution to our stockholders. 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 well as shares of common stock underlying an option to purchase up to 145,000 shares of our common stock that was granted as an inducement grant. 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. 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.

Comprehensive tax reform in the United States could adversely affect our business and financial condition.

The Tax Cuts and Jobs Act (the "TJCA") was enacted on December 22, 2017 in the United States. The TJCA contains significant changes to corporate taxation, including reduction of the U.S. corporate tax rate from 35% to 21%, elimination of U.S. tax on foreign earnings (subject to certain important exceptions), one-time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, limitation of the tax deduction for interest expense, immediate deductions for certain new investments instead of deductions for depreciation expense over time, and modifying or repealing many business deductions and credits.

Notwithstanding the reduction in the corporate income tax rate, the overall impact of the TJCA is uncertain, and our business and financial condition could be adversely affected. We are still in the process of evaluating the TJCA and do not know the full effect it will have on our business, including our consolidated financial statements. The TJCA is complex and far-reaching and we cannot predict with certainty the impact its enactment will have on us. Moreover, that effect, whether adverse or favorable, may not become evident for some period of time. Further, we urge stockholders to consult with their legal and tax advisors with respect to the Tax Reform Act and the potential tax consequences of investing in our common stock.

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 have completed additional analyses through December 31, 2017 and determined that an ownership change occurred subsequent to September 7, 2011 and are in the process of analyzing the impact to our NOL and research and development tax credit carryforwards. 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 24,494 square feet of office and laboratory space under an operating lease that expires in 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, 2017:		
First Quarter	\$ 4.45	\$ 2.25
Second Quarter	\$ 3.75	\$ 3.00
Third Quarter	\$ 5.35	\$ 2.30
Fourth Quarter	\$ 6.50	\$ 3.30

	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

Holdings of Record

As of March 15, 2018, there were approximately 59 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.

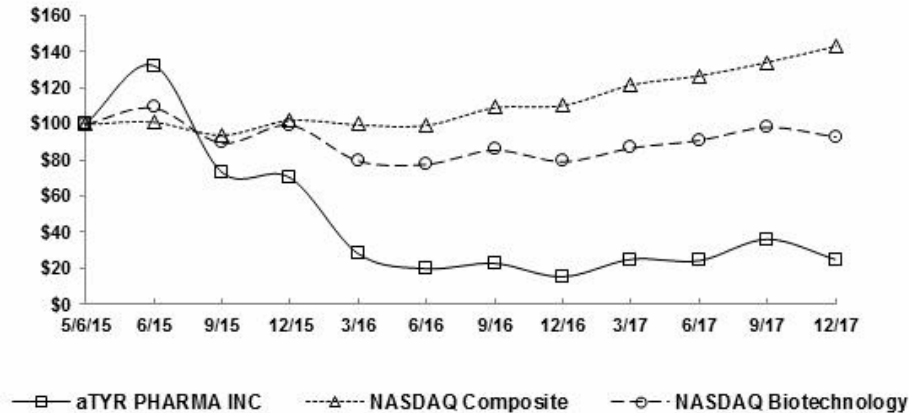
Performance Graph

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, 2017 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

COMPARISON OF 32 MONTH CUMULATIVE TOTAL RETURN*

Among aTYR PHARMA INC, the NASDAQ Composite Index and the NASDAQ Biotechnology Index



*\$100 invested on 5/6/15 in stock or 4/30/15 in index, including reinvestment of dividends. Fiscal year ending December 31.

Recent Sales of Unregistered Securities

During the year ended December 31, 2017, 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 year ended December 31, 2017.

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,		
	2017	2016	2015
Statements of Operations Data:			
Loss from operations	\$ (47,145)	\$ (57,940)	\$ (47,616)
Net loss	(48,207)	(57,855)	(47,973)
Comprehensive loss	(48,251)	(57,760)	(48,144)
Net loss per share, basic and diluted	\$ (1.87)	\$ (2.44)	\$ (3.03)
Weighted average shares outstanding, basic and diluted	25,799,853	23,681,019	15,838,353

	As of December 31,		
	2017	2016	2015
Consolidated Balance Sheet Data:			
Cash, cash equivalents and available-for-sale investments	\$ 85,119	\$ 76,149	\$ 125,349
Total assets	89,355	80,524	129,675
Working capital	76,594	66,243	85,802
Long-term debt, net of current portion and issuance costs	14,719	9,198	1,776
Accumulated deficit	(264,186)	(215,979)	(158,124)
Total stockholders' equity (deficit)	64,245	62,801	115,050

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 using our knowledge of tRNA synthetase biology. We have discovered novel extracellular functions of proteins derived from a number of tRNA synthetase genes, a family of more than 20 genes that influence immune function, and other activities, in previously unknown ways. Built on more than a decade of foundational science on extracellular tRNA synthetase biology and its effect on immune responses, we have built a global intellectual property estate directed to all 20 human tRNA synthetases as well as our product candidates.

Today, we focus on the therapeutic translation of the Resokine pathway, comprised of extracellular proteins derived from the histidyl tRNA synthetase (HARS) gene family, which has fueled a pipeline of novel drug candidate programs addressing disease areas of high unmet medical need, including cancer and lung disease. We refer to these proteins as Resokine proteins. Our current programs include:

ORCA

Our ORCA program is a preclinical immune-oncology research program that targets the Resokine pathway using antibodies to bind to Resokine in tumor settings. We believe tumors, across multiple tumor types, may utilize Resokine to aid in the evasion of host anti-tumor immune responses. We have evaluated the therapeutic potential of targeting this novel pathway in multiple *in vitro* and *in vivo* tumor models, in comparison to and in combination with incumbent check-point modulators. Based on the tumor model data, we believe that targeting this pathway can reduce or, in some cases, reverse tumor growth either as a monotherapy or in combination therapy.

ATYR1923 (iMod.Fc)

Our scientists successfully engineered the first fusion protein with a Resokine protein, ATYR1923, to provide designed properties to enhance the immuno-modulatory aspects *in vivo*. We plan to develop ATYR1923 as a potential therapeutic for patients with interstitial lung diseases (ILD). This fusion protein, which utilizes the Fc region of an antibody, also potentially represents a novel Fc fusion platform for future tRNA synthetase based therapies. We are currently conducting a first-in-human Phase 1 clinical trial of ATYR1923. This randomized, double-blind, placebo-controlled study will investigate the safety, tolerability, immunogenicity, and pharmacokinetics of intravenous ATYR1923 in healthy volunteers. We anticipate learning more about the safety profile and tolerability of ATYR1923 as well as some characteristics of its pharmacokinetics and dosing potential. In parallel, we are expanding our knowledge base of the therapeutic potential of ATYR1923 by conducting several *in vivo* and *in vitro* models to further elucidate its potential clinical utility. These data, as well as the Phase 1 clinical trial results, will help inform selection of the indication for future clinical trials for our ATYR1923 program.

ATYR1940 (Resolaris)

We internally discovered and developed ATYR1940, our first therapeutic candidate based on a protein naturally secreted from muscle (Resokine) that may act to influence T-cell activation at the tissue level to promote healthier muscle. There is potential that ATYR1940 may translate into an innovative therapeutic for rare genetic myopathies with an immune component, including limb-girdle muscular dystrophy (LGMD), facioscapulohumeral muscular dystrophy (FSHD), and Duchenne muscular dystrophy (DMD). We collected evidence that supports applicability of ATYR1940 as an example of adding back a protein that is insufficiently produced by the human body to potentially counteract disease.

Our 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 250 issued patents or allowed patent applications that are owned or exclusively licensed by us, including over 300 potential protein compositions.

Since our inception in 2005, we have devoted substantially all of our resources to the therapeutic potential of tRNA synthetase biology, including the preclinical development of and clinical trials for ATYR1940, 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, 2017, have funded our operations primarily with the aggregate proceeds from the sales

of our common stock in our initial public offering (IPO), private placements of our capital stock, convertible promissory notes, commercial bank debt and a convertible promissory note issued to our landlord and term loans.

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.

In August 2017, we completed our Private Placement in which a select group of institutional investors and other accredited investors, certain of whom are affiliated with our directors and officers, purchased our equity securities. Pursuant to the Securities Purchase Agreement, we sold (i) an aggregate of 5,872,120 shares of our common stock at a price of \$2.65 per unit (each common stock unit consisting of one share of our common stock and a warrant to purchase 0.375 shares of our common stock), (ii) an aggregate of 2,285,952 Preferred Shares at a price of \$13.25 per unit (each preferred stock unit consisting of one Preferred Share and a warrant to purchase 1.875 shares of our common stock) and (iii) warrants to purchase up to an aggregate of 6,488,205 shares of our common stock at an exercise price of \$4.64 per share that expire on December 31, 2019. The gross proceeds from the Private Placement were \$45.8 million. After giving effect to the costs related to the Private Placement, the net proceeds were \$42.5 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, 2017, 2016 and 2015, we have incurred consolidated net losses of \$48.2 million, \$57.9 million and \$48.0 million, respectively. As of December 31, 2017, we had an accumulated deficit of \$264.2 million.

Substantially all of our net losses resulted from costs incurred in connection with our development of and clinical trials for ATYR1940 and ATYR1923, our other research and development programs (including ORCA) and from general and administrative costs associated with our operations. We expect to continue to incur significant expenses and operating losses for the foreseeable future, at least until we apply for and receive regulatory approval for our product candidates 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 fluctuate in connection with our ongoing activities as we:

- conduct clinical trials of ATYR1923 and any additional product candidates we may develop, including any product candidates from our ORCA program;
- 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. 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. 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.

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, 2017. 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 ATYR1940, ATYR1923, research and development activities related to our ORCA program and to research efforts targeting the potential therapeutic application of other Physiocrine-based immuno-modulators (including funding of our research collaborations with The Scripps Research Institute). 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 in the current year and will consist primarily of costs related to advancing our ORCA program, including antibody development and CMC activities, advancing our ATYR1923 program into clinical trials and research, discovery and development activities relating to our discovery engine for therapeutics based on tRNA synthetase biology, including our ORCA program.

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 our product candidates. 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 programs or 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 Term Loans outstanding with Silicon Valley Bank (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 our product candidates and the manufacture of our product candidates 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. 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. We follow Accounting Standards Codification (ASC) Topic 718, *Compensation – Stock Compensation* and ASC 505-50 *Equity Based Payments to Non-employees* as guidance for accounting modifications.

Results of Operations

Comparison of the Years Ended December 31, 2017 and 2016

The following table summarizes our results of operations for the years ended December 31, 2017 and 2016 (in thousands):

	Years Ended December 31,		Increase / (Decrease)
	2017	2016	
Research and development expenses	\$ 30,067	\$ 42,846	\$ (12,779)
General and administrative expenses	17,078	15,094	1,984
Other income (expense)	(1,062)	36	(1,098)

Research and development expenses. Research and development expenses were \$30.1 million and \$42.8 million for the years ended December 31, 2017 and 2016, respectively. The decrease of \$12.8 million was due primarily to a \$9.6 million decrease related to manufacturing costs incurred in support of ATYR1940, a \$6.7 million decrease related to ATYR1940 clinical trial costs, a \$0.5 million decrease in discovery projects, and a \$0.5 million decrease in non-cash stock-based compensation expense. The decrease was partially offset by an increase of \$1.3 million related to ATYR1923 phase 1 clinical studies, a \$1.2 million increase related to research and non-clinical development costs incurred for ATYR1923, a \$1.1 million increase related to ORCA pre-clinical and research activities, an increase of \$0.8 million related to manufacturing costs incurred in support of ATYR1923.

General and administrative expenses. General and administrative expenses were \$17.1 million and \$15.1 million for the years ended December 31, 2017 and 2016, respectively. The increase of \$2.0 million was due primarily to a \$2.2 million increase in non-cash stock-based compensation expense related to executive transitions, which was partially offset by a reduction of \$0.2 million in professional fees.

Other income (expense). Other income (expense) was \$(1.1) million and \$36,000 for the years ended December 31, 2017 and 2016, respectively. The change was primarily a result of increased interest expense related to our Term Loans.

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):

	Year Ended December 31,		Increase / (Decrease)
	2016	2015	
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 ATYR1940, a \$2.4 million increase in manufacturing development costs for ATYR1923, a \$2.0 million increase in other pre-clinical development costs, a \$1.2 million increase related to cGMP manufacturing of ATYR1940 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 debt balance.

Liquidity and Capital Resources

We have incurred losses and negative cash flows from operations since our inception. As of December 31, 2017, we had an accumulated deficit of \$264.2 million and we expect to continue to incur net losses for the foreseeable future. As of December 31, 2017, we had cash, cash equivalents and available-for-sale investments of \$85.1 million. We believe that our existing cash and cash equivalents as of December 31, 2017 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, 2017, we have funded our operations primarily with aggregate proceeds from the sales of our common stock through our IPO, the private placement of our capital stock, promissory notes, venture debt, a convertible promissory note issued to our landlord and term loans.

Debt Financing

In November 2016, we entered into a loan and security agreement (the Loan Agreement) with SVB and Solar to borrow to \$20.0 million, issuable in three separate tranches of \$10.0 million, \$5.0 million and \$5.0 million, respectively. The first tranche of \$10.0 million was funded on November 18, 2016 (Term A Loan). Under the Term A Loan, we received cash proceeds of \$7.3 million, net of a \$2.6 million repayment of the principal, accrued interest and \$0.5 million final payment under our previous \$10.0 million loan and security agreement with SVB (SVB Loan). We did not pay any termination or other fees in connection with the repayment of amounts due under the SVB Loan. The second tranche of \$5.0 million was funded on June 30, 2017 (Term B Loan). Under the Term B Loan, we received cash proceeds of \$4.9 million, net of debt issuance costs of \$0.1 million.

In December 2017, we entered into an amendment of the Loan Agreement which modified the milestone requirements for the draw of the third tranche of the loan to include Australia as a qualifying geography for the initiation of a Phase 1 clinical trial for ATYR1923. In connection with the amendment to the Loan Agreement, the third tranche of \$5.0 million was funded on December 22, 2017 (Term C Loan). We received cash proceeds of \$4.9 million, net of debt issuance costs of \$0.1 million.

Pursuant to the Loan Agreement, as amended, we were originally obligated to make interest only payments through December 1, 2017, followed by consecutive equal monthly payments of principal and interest in arrears through the maturity date of November 18, 2020. The interest only period was extended to June 1, 2018 upon achievement of certain milestones as set forth in the Loan Agreement, as amended. The Term A Loan, Term B Loan and Term C Loan (collectively, as Term Loans) bear 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%. A final payment equal to 8.75% of the funded amounts is payable when the Term Loans become due or upon the prepayment of the respective outstanding balance. 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.

In connection with the Term A 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. In connection with the Term B Loan, we issued warrants to each of SVB and Solar to purchase an aggregate of 20,833 shares of our common stock with an exercise price of \$3.60 per share. In connection with the Term C Loan, we issued warrants to each of SVB and Solar to purchase an aggregate of 20,188 shares of our common stock with an exercise price of \$3.72 per share. The warrants are immediately exercisable and have a maximum contractual term of seven years.

Cash Flows

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

	Year Ended December 31,		
	2017	2016	2015
Net cash provided by (used in):			
Operating activities	\$ (42,353)	\$ (52,861)	\$ (36,797)
Investing activities	(27,648)	33,527	(71,994)
Financing activities	52,704	4,697	147,917
Net decrease in cash	<u>\$ (17,297)</u>	<u>\$ (14,637)</u>	<u>\$ 39,126</u>

Operating activities. Net cash used in operating activities was \$42.4 million, \$52.9 million and \$36.8 million for the years ended December 31, 2017, 2016 and 2015, 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, 2017 related to non-cash charges including: \$0.7 million for depreciation and amortization and \$6.8 million for stock-based compensation and an increase in our net operating assets and liabilities of \$1.7 million. 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, \$5.0 million for stock-based compensation, and an increase in our net operating assets and liabilities of \$1.4 million. 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 The Scripps Research Institute (TSRI) and a decrease in our net operating assets and liabilities of \$3.3 million.

Investing activities. Net cash used in investing activities for the year ended December 31, 2017 consisted of \$26.3 million of net purchases of investment securities and \$1.3 million of property and equipment purchases. 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.

Financing activities. Net cash provided by financing activities during the year ended December 31, 2017 was \$52.7 million and consisted primarily of \$42.5 million of proceeds from the private placement, net of offering costs paid in the period and \$9.9 million from the Term B Loan and Term C Loan, net of issuance costs. Net cash provided by financing activities for the year ended December 31, 2016 was \$4.7 million and consisted primarily of \$9.7 million from the Term A Loan, net of issuance costs offset by \$5.2 million of principal payments on the SVB Loan. 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.

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 our ORCA program, advance ATYR1923 in clinical development, continue our research and development activities with respect to potential tRNA synthetase-based therapeutics, and seek marketing approval for 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 advance our ORCA program, including antibody development and CMC activities;
- our ability to initiate, and the progress and results of, our planned clinical trials of ATYR1923;
- 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, 2017:

	Total	Payments Due by Period			
		Less than 1 Year	1-3 Years	3-5 Years	More than 5 Years
		(in thousands)			
Term Loans, principal payments only	\$ 20,000	\$ 5,333	\$ 14,667	\$ —	\$ —
Operating lease (1)	1,528	1,108	420	—	—
Total	\$ 21,528	\$ 6,441	\$ 15,087	\$ —	\$ —

- (1) Our operating lease obligations relate to our corporate headquarters in San Diego, California. We have 24,494 square feet of office and laboratory space under an operating lease that expires in May 2019.

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, 2017, 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 are currently evaluating four early stage discovery projects at TSRI and are evaluating the level of funding we will direct to these projects beyond May 31, 2018 as part of our portfolio prioritization process.

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 ATYR1923. In the next 12 months, based on statements of work, we are committed to pay the third party contract manufacturing organization approximately \$1.6 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.

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, 2017, we had cash and cash equivalents, and available-for-sale investments totaling \$85.1 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 one years. If interest rates were to increase instantaneously and uniformly by 100 basis points, compared to interest rates as of December 31, 2017, the increase would not have had a material effect on our results of operations.

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 Loans bear 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 \$0.2 million annually and would not materially affect our results of operations.

Foreign Currency Exchange Risk

We incur expenses, including for clinical research organizations and clinical trial sites, outside the United States based on contractual obligations denominated in currencies other than the U.S. dollar, including Pounds Sterling, Euro and Australian dollar. 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. 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

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of aTyr Pharma, Inc. (the Company) as of December 31, 2017 and 2016, 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, 2017, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2017 and 2016, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2017, in conformity with U.S. generally accepted accounting principles.

Basis for Opinion

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

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

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

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2008.

San Diego, California

March 20, 2018

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

	December 31,	
	2017	2016
Assets		
Current assets:		
Cash and cash equivalents	\$ 21,091	\$ 38,388
Available-for-sale investments, short-term	64,028	33,759
Prepaid expenses and other assets	1,866	2,621
Total current assets	86,985	74,768
Available-for-sale investments, long-term	—	4,002
Property and equipment, net	2,280	1,421
Other assets	90	333
Total assets	\$ 89,355	\$ 80,524
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	\$ 2,276	\$ 2,606
Accrued expenses	3,103	5,450
Current portion of deferred rent	—	130
Current portion of long-term debt, net of issuance costs and discount	5,012	339
Total current liabilities	10,391	8,525
Long-term debt, net of current portion and issuance costs and discount	14,719	9,198
Commitments and contingencies (Note 5)		
Stockholders' equity:		
Preferred stock, \$0.001 par value; undesignated authorized shares – 5,000,000 at December 31, 2017 and 2016, respectively; Class X Convertible Preferred Stock issued and outstanding shares – 2,285,952 and no shares at December 31, 2017 and 2016, respectively	2	—
Common stock, \$0.001 par value; authorized shares – 150,000,000 as of December 31, 2017 and 2016, respectively; issued and outstanding shares – 29,789,162 and 23,744,832 as of December 31, 2017 and 2016, respectively	30	24
Additional paid-in capital	328,519	278,832
Accumulated other comprehensive loss	(120)	(76)
Accumulated deficit	(264,186)	(215,979)
Total stockholders' equity	64,245	62,801
Total liabilities and stockholders' equity	\$ 89,355	\$ 80,524

See accompanying notes.

aTyr Pharma, Inc.
Consolidated Statements of Operations
(in thousands, except share and per share data)

	Year Ended December 31,		
	2017	2016	2015
Operating expenses:			
Research and development	\$ 30,067	\$ 42,846	\$ 34,504
General and administrative	17,078	15,094	13,112
Total operating expenses	47,145	57,940	47,616
Loss from operations	(47,145)	(57,940)	(47,616)
Other income (expense), net			
Other income (expense), net	(1,062)	65	(386)
Loss on extinguishment of debt	—	(29)	—
Change in fair value of warrant liabilities	—	—	29
Total other income (expense)	(1,062)	36	(357)
Loss before income taxes	(48,207)	(57,904)	(47,973)
Income tax benefit	—	49	—
Net loss	(48,207)	(57,855)	(47,973)
Accretion to redemption value of redeemable convertible preferred stock	—	—	(15)
Net loss per share attributable to common stockholders, basic and diluted	(48,207)	(57,855)	(47,988)
Net loss per share, basic and diluted	\$ (1.87)	\$ (2.44)	\$ (3.03)
Weighted average common shares outstanding, basic and diluted	25,799,853	23,681,019	15,838,353

See accompanying notes.

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

	Year Ended December 31,		
	2017	2016	2015
Net loss	\$ (48,207)	\$ (57,855)	\$ (47,973)
Other comprehensive gain (loss):			
Change in unrealized gain (loss) on available for sale investments, net of tax	(44)	95	(171)
Comprehensive loss	\$ (48,251)	\$ (57,760)	\$ (48,144)

See accompanying notes.

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

	Redeemable Convertible Preferred Stock		Convertible Preferred Stock		Common Stock		Additional Paid-In Capital	Stockholder Note Receivable	Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount	Shares	Amount					
	Balance as of December 31, 2014	73,487,415	\$ 95,619	—	\$ —	909,880					
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 and release of restricted stock units	—	—	—	—	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
Exercise of common stock options and release of restricted stock units	—	—	—	—	111,039	—	186	—	—	—	186

Issuance of common stock pursuant to employee stock purchase plan	—	—	—	—	61,171	—	175	—	—	—	175
Issuance of common stock and preferred stock from private placement, net of offering costs	—	—	2,285,952	2	5,872,120	6	42,231	—	—	—	42,239
Issuance of warrants related to term loan	—	—	—	—	—	—	263	—	—	—	263
Changes in share repurchase liability	—	—	—	—	—	—	48	—	—	—	48
Stock-based compensation	—	—	—	—	—	—	6,784	—	—	—	6,784
Net unrealized loss on investments	—	—	—	—	—	—	—	—	(44)	—	(44)
Net loss	—	—	—	—	—	—	—	—	—	(48,207)	(48,207)
Balance as of December 31, 2017	—	—	<u>2,285,952</u>	<u>\$ 2</u>	<u>29,789,162</u>	<u>\$ 30</u>	<u>\$ 328,519</u>	<u>\$ —</u>	<u>\$ (120)</u>	<u>\$ (264,186)</u>	<u>\$ 64,245</u>

See accompanying notes.

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

	Year Ended December 31,		
	2017	2016	2015
Cash flows from operating activities:			
Net loss	\$ (48,207)	\$ (57,855)	\$ (47,973)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	713	900	869
Issuance of common stock for technology	—	—	1,411
Stock-based compensation	6,784	5,029	4,856
Accretion of debt discount	192	173	297
Loss on debt extinguishment	—	29	—
Change in fair value of preferred stock warrant liability	—	—	(29)
Amortization of premium of available-for-sale investment securities	14	531	789
Deferred rent	(130)	(315)	(295)
Changes in operating assets and liabilities			
Prepaid expenses and other assets	761	(421)	(666)
Accounts payable and accrued expenses	(2,491)	(932)	3,944
Net cash used in operating activities	(42,364)	(52,861)	(36,797)
Cash flows from investing activities:			
Purchases of property and equipment	(1,312)	(600)	(664)
Purchases of available-for-sale investment securities	(77,672)	(28,089)	(109,445)
Maturities of available-for-sale investment securities	51,347	62,216	38,115
Net cash (used in) provided by investing activities	(27,637)	33,527	(71,994)
Cash flows from financing activities:			
Proceeds from issuance of preferred stock for cash, net of issuance costs	—	—	75,648
Proceeds from issuance of common stock through initial public offering, net of offering costs	—	—	76,902
Proceeds from issuance of common stock through option exercises	186	20	604
Proceeds through employee stock purchase plan	175	143	—
Proceeds from borrowing, net	9,866	9,736	—
Proceeds from issuance of securities through private placement, net of issuance costs	42,477	—	—
Repayments on loans payable	—	(5,202)	(3,237)
Repayments of convertible debt	—	—	(2,000)
Net cash provided by financing activities	52,704	4,697	147,917
Net change in cash and cash equivalents	(17,297)	(14,637)	39,126
Cash and cash equivalents at beginning of period	38,388	53,025	13,899
Cash and cash equivalents at the end of period	<u>\$ 21,091</u>	<u>\$ 38,388</u>	<u>\$ 53,025</u>
Supplemental disclosure of cash flow information:			
Interest paid	<u>\$ 1,000</u>	<u>\$ 225</u>	<u>\$ 925</u>
Supplemental schedule of noncash investing and financing activities:			
Issuance of warrants in connection with borrowings	<u>\$ 263</u>	<u>\$ 217</u>	<u>\$ —</u>
Changes in share repurchase liability	<u>\$ 48</u>	<u>\$ 102</u>	<u>\$ (120)</u>

See accompanying notes.

Notes to Consolidated Financial Statements

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 using our knowledge of tRNA synthetase biology.

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 trials 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, 2017, we held an aggregate total of \$64.0 million of investment securities which consisted of corporate debt securities, asset-backed securities, all of which will mature in less than one year and there was a \$0.1 million difference between the amortized cost and fair value of these investment securities. As of December 31, 2016, we held \$37.8 million of corporate debt securities, all of which mature in less than one year, and there was \$27,000 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 clinical research organizations (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. Historically, our estimated accrued liabilities have approximated actual expenses incurred. Subsequent changes in estimates may result in a material change in our accruals.

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. 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 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 3,685, 25,984 and 61,814 shares subject to repurchase from the weighted average number of common shares outstanding for the years ended December 31, 2017, 2016 and 2015, 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 convertible preferred stock, warrants for common stock, options and restricted stock units outstanding under our stock option plan and estimated shares to be purchased under our employee stock purchase 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,		
	2017	2016	2015
Class X Convertible Preferred Stock (if-converted)	11,429,760	—	—
Warrants for common stock	6,682,708	121,512	25,970
Common stock options and restricted stock units	4,666,359	4,091,701	2,625,280
Employee stock purchase plan	31,086	36,836	17,363
	<u>22,809,913</u>	<u>4,250,049</u>	<u>2,668,613</u>

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

	Year Ended December 31,		
	2017	2016	2015
Numerator:			
Consolidated net loss	\$ (48,207)	\$ (57,855)	\$ (47,973)
Accretion to redemption value	—	—	(15)
Net loss attributable to common stockholders	<u>(48,207)</u>	<u>(57,855)</u>	<u>(47,988)</u>
Denominator:			
Weighted average common shares outstanding	25,803,538	23,707,003	15,900,167
Weighted average common shares subject to repurchase	(3,685)	(25,984)	(61,814)
Weighted average common shares outstanding - basic and diluted	<u>25,799,853</u>	<u>23,681,019</u>	<u>15,838,353</u>
Net loss per share - basic and diluted	<u>\$ (1.87)</u>	<u>\$ (2.44)</u>	<u>\$ (3.03)</u>

Convertible Preferred Stock

We apply the relevant accounting standards to distinguish liabilities from equity when assessing the classification and measurement of preferred stock. Preferred shares subject to mandatory redemptions are considered liabilities and measured at fair value. Conditionally redeemable preferred shares are considered temporary equity. All other preferred shares are considered as stockholders' equity. None of our outstanding preferred stock has redemption features.

Derivative Financial Instruments

We do not use derivative instruments to hedge exposures to cash flow, market, or foreign currency risks. We evaluate all of our financial instruments, including warrants, to determine if such instruments are derivatives or contain features that qualify as embedded derivatives. We generally use the Black-Scholes option-pricing model to value the derivative instruments at inception and subsequent valuation dates. The classification of derivative instruments, including whether such instruments should be recorded as liabilities or as equity, is re-assessed at the end of each reporting period.

Recent Accounting Pronouncements

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, 2017, and interim periods within those annual fiscal years. Early adoption is permitted for certain provisions. The adoption of ASU 2016-01 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 be 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 May 2017, the FASB issued ASU 2017-09, *Compensation-Stock Compensation (Topic 718): Scope of Modification Accounting*, to provide guidance about which changes to the terms or conditions of a share-based payment award require an entity to apply modification accounting in Topic 718. ASU 2017-09 will be effective for the annual periods beginning after December 15, 2017. Early adoption is permitted. We do not expect that the adoption of ASU 2017-09 will 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 Loans approximate 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 asset-backed securities, commercial paper, and corporate debt 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, 2017:				
Assets:				
Current:				
Cash equivalents	\$ 9,070	\$ 9,070	\$ —	\$ —
Available-for-sale investments, short-term:				
Asset-backed securities	6,497	—	6,497	—
Commercial paper	21,943	—	21,943	—
Corporate debt securities	18,260	—	18,260	—
United States Treasury securities	17,328	17,328	—	—
Sub-total short-term investments	64,028	17,328	46,700	—
Total assets measured at fair value	\$ 73,098	\$ 26,398	\$ 46,700	\$ —
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, 2017 and 2016, available-for-sale investments are detailed as follows (in thousands):

	December 31, 2017			
	Gross Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Market Value
Available-for-sale investments, short-term:				
Asset-backed securities	\$ 6,501	—	(4)	\$ 6,497
Commercial paper	21,943	—	—	21,943
Corporate debt securities	18,286	—	(26)	18,260
United States Treasury securities	17,368	—	(40)	17,328
	<u>\$ 64,098</u>	<u>\$ —</u>	<u>\$ (70)</u>	<u>\$ 64,028</u>
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
	<u>\$ 33,787</u>	<u>\$ 1</u>	<u>\$ (29)</u>	<u>\$ 33,759</u>
Available-for-sale investments, long-term:				
Asset-backed securities	\$ 4,001	\$ 1	\$ —	\$ 4,002
	<u>\$ 4,001</u>	<u>\$ 1</u>	<u>\$ —</u>	<u>\$ 4,002</u>

As of December 31, 2017, all available-for-sale investments have contractual maturity dates less than one year. As of December 31, 2017, there are 20 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, 2017.

4. Balance Sheet Details

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

	December 31,	
	2017	2016
Computer and office equipment	\$ 425	\$ 401
Scientific and laboratory equipment	5,494	3,965
Tenant improvements	1,706	1,687
	7,625	6,053
Less accumulated depreciation and amortization	(5,345)	(4,632)
	<u>\$ 2,280</u>	<u>\$ 1,421</u>

Accrued expenses consist of the following (in thousands):

	December 31,	
	2017	2016
Accrued salaries, wages and benefits	1,920	1,977
Other accrued expenses (1)	1,183	3,473
	<u>\$ 3,103</u>	<u>\$ 5,450</u>

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

5. Debt, Commitments and Contingencies

Term Loans

In November 2016, we entered into a loan and security agreement (the Loan Agreement) with Silicon Valley Bank (SVB) and Solar Capital Ltd. (Solar) to borrow up to \$20.0 million, issuable in three separate tranches of \$10.0 million, \$5.0 million and \$5.0 million, respectively. The first tranche of \$10.0 million was funded in November 2016 (Term A Loan). Under the Term A Loan, 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 under our previous \$10.0 million loan and security agreement with SVB (SVB Loan). We did not pay any termination or other fees in connection with the repayment of amounts due under the SVB Loan.

In June 2017 and December 2017, we entered amendments to the Loan Agreement which modified certain conditions under which we may receive and repay the term loans under the Loan Agreement. The second (Term B) and third (Term C) tranche of \$5.0 million each were funded in June 2017 and December 2017, respectively. We received total cash proceeds of \$9.9 million, net of debt issuance costs of \$0.1 million for both tranches. The amendments to the Loan Agreement were not a result of a troubled debt restructuring and did not result in modifications to the terms that were substantially different.

Under the Loan Agreement, we were originally obligated to make interest only payments through December 1, 2017, followed by consecutive equal monthly payments of principal and interest in arrears through the maturity date of November 18, 2020. With the Loan Agreement, as amended, the interest only period was extended to June 1, 2018. The Term A Loan, Term B Loan and Term C Loan (collectively, the Term Loans) bear 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%. A final payment equal to 8.75% of the funded amounts is payable when the Term Loans become due or upon the prepayment of the respective outstanding balance. 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, as well as any non-usage fees.

The obligations under the Term Loans are secured by liens on our tangible personal property and we agreed to not encumber any of our intellectual property. The Term Loans include a material adverse change clause, which enables the Lenders to require immediate repayment of the outstanding debt. The material adverse change clause covers a material impairment in the perfection or priority of the lenders' lien in the underlying collateral or in the value of such collateral, material adverse change in business operations or condition or material impairment of our prospects for repayment of any portion of the remaining debt obligation.

As of December 31, 2017, the carrying value of our Term Loans consist of \$20.0 million principal outstanding less the debt issuance costs of \$0.9 million. The debt issuance costs have been recorded as a debt discount which are being accreted to interest expense over the life of the Term Loans. The final maturity payment of \$1.8 million is accruing over the life of the Term Loans through interest expense.

In connection with the Term A 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. In connection with the Term B Loan, we issued warrants to each of SVB and Solar to purchase an aggregate of 20,833 shares of our common stock with an exercise price of \$3.60 per share. In connection with the Term C Loan, we issued warrants to each of SVB and Solar to purchase an aggregate of 20,188 shares of our common stock with an exercise price of \$3.72 per share. The warrants are immediately exercisable and have a maximum contractual term of seven years. The aggregate fair value of the warrants was determined to be \$0.5 million using the Black-Scholes option pricing model and was recorded as debt discount which are being accreted to interest expense over the life of Term Loans.

Term loans and unamortized discount balances are as follows (in thousands):

	December 31,	
	2017	2016
Long-term debt	\$ 20,000	\$ 10,000
Less debt issuance costs and discount	(345)	(463)
Long-term debt, net of issuance costs and discount	19,655	9,537
Less current portion of long-term debt	(5,333)	(339)
Add accrual of final payment	397	—
Long-term debt, net of current portion and issuance costs and discount	<u>\$ 14,719</u>	<u>\$ 9,198</u>
Current portion of long-term debt	\$ 5,333	\$ 339
Less current portion of debt issuance costs and discount	(321)	—
Current portion of long-term debt, net of issuance costs and discount	<u>\$ 5,012</u>	<u>\$ 339</u>

Future principal payments for the Term Loans are as follows (in thousands):

	December 31, 2017
2018	\$ 5,333
2019	8,000
2020	6,667
	<u>\$ 20,000</u>

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. In January 2017, we extended the lease for two years to May 2019.

In April 2017, we amended our facility lease to include an additional 7,411 square feet through May 2019 for a total additional commitment of \$0.7 million.

Rent expense for the years ended December 31, 2017, 2016 and 2015 was \$0.9 million, \$0.5 million and \$0.4 million, respectively.

As of December 31, 2017, future minimum payments under the non-cancelable operating lease are as follows (in thousands):

	Operating Lease
2018	\$ 1,108
2019	420
	<u>\$ 1,528</u>

Research Agreements and Funding Obligations (Related Party Transactions)

We provide funding to The Scripps Research Institute (TSRI) pursuant to a research funding and option agreement to conduct certain research activities. We have entered into additional amendments to our research funding and option agreement in 2016 and 2017 to provide additional funding to TSRI. During the years ended December 31, 2017, 2016 and 2015, excluding the fair value of the common stock issued to TSRI, we recognized expense under the agreement in the amount of \$1.8 million, \$1.6 million and \$0.7 million, respectively. Paul Schimmel, Ph.D., a member of our board of directors, is a board and faculty member at TSRI and such payments fund a portion of his research activities conducted at TSRI.

During the years ended December 31, 2017, 2016 and 2015, we provided charitable donations to the National Foundation for Cancer Research of \$0.2 million, \$0.4 million and \$0.4 million, respectively. 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

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 ATYR1923. 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, based on statements of work, we are committed to pay the third party contract manufacturing organization approximately \$1.6 million based on development and production milestones. For the year ended December 31, 2017 and 2016, expenses associated with this agreement were \$2.8 million and \$1.1 million, respectively.

6. Stockholders' Equity

Common Stock

Private Placement of Common Stock, Convertible Preferred Shares and Common Stock Warrants

On August 27, 2017, we entered into a Securities Purchase Agreement (Securities Purchase Agreement) for a private placement (Private Placement) with a select group of institutional investors, including Viking Global Opportunities Illiquid Investments Sub-Master, LP (VGO Fund) and other accredited investors, certain of whom are affiliated with our directors and officers (collectively, the Purchasers). Pursuant to the Securities Purchase Agreement, (i) VGO Fund purchased 1,777,784 shares of our common stock, par value \$0.001 per share (the Common Shares), at a price of \$2.65 per share, 2,285,952 shares of our Class X Convertible Preferred Stock (the Preferred Shares or Preferred Stock, and together with the Common Shares, the Shares), par value \$0.001 per share, at a price of \$13.25 per share, and warrants to purchase up to that number of additional shares of Common Stock equal to thirty seven and one half percent (37.5%) of the number of Shares purchased by VGO Fund on an if-converted to common stock basis (rounded up to the nearest whole share), and (ii) the remaining Purchasers purchased an aggregate of 4,094,336 shares of our Common Shares, at a price of \$2.65 per share, and warrants to purchase up to that number of additional shares of Common Stock equal to thirty-seven and one half percent (37.5%) of the number of Common Shares purchased by such Purchaser (rounded up to the nearest whole share). The Private Placement closed on August 31, 2017 for gross proceeds of \$45.8 million, and after giving effect to costs related to the Private Placement, net proceeds of \$42.5 million.

Each share of Preferred Stock is convertible into five shares of our common stock. VGO Fund will be prohibited from converting the Preferred Stock into shares of our common stock if, as a result of such conversion, VGO Fund, together with its affiliates, would own more than 9.50% of the shares of our common stock then issued and outstanding, which percentage may change at VGO Fund's election upon 61 days' notice to us to (i) any other number less than or equal to 19.99% or (ii) subject to approval of our stockholders to the extent required in accordance with the NASDAQ Global Market rules, any number in excess of 19.99%.

Holders of outstanding Preferred Stock are entitled to receive a dividend (on an if-converted to common stock basis), if we at any time pay a stock dividend equal to and in the same form as a dividend paid to holders of Common Shares.

In the event of our liquidation, dissolution or winding up, holders of Preferred Stock will participate in any distribution of proceeds, pro rata based on the number of shares held by each such holder on an if-converted basis. The Preferred Shares have no voting rights.

We evaluated the Preferred Stock for liability or equity classification under ASC 480, *Distinguishing Liabilities from Equity* (ASC 480), and determined that equity treatment was appropriate because the Preferred Stock did not meet the definition of the liability instruments defined thereunder for convertible instruments. Specifically, the Preferred Stock are not mandatorily redeemable and do not embody an obligation to buy back the shares outside of our control in a manner that could require the transfer of assets. Additionally, we determined that the Preferred Stock would be recorded as permanent equity, not temporary equity, based on the guidance of ASC 480 given that they are not redeemable for cash or other assets (i) on a fixed or determinable date, (ii) at the option of the holder, and (iii) upon the occurrence of an event that is not solely within control of the Company.

We also evaluated the Preferred Stock in accordance with the provisions of ASC 815, *Derivatives and Hedging*, including the consideration of embedded derivatives requiring bifurcation from the equity host. Based on this assessment, we determined that the conversion option is closely related to the equity host, and thus, bifurcation is not required.

The issuance of convertible preferred stock could generate a beneficial conversion feature (BCF), which arises when a debt or equity security is issued with an embedded conversion option that is beneficial to the investor (or in-the-money) at inception because the conversion option has an effective strike price that is less than the market price of the underlying stock on the commitment date. The fair value of our common stock was \$2.37 on August 31, 2017, the commitment date, using the Black-Scholes valuation model. After the proceeds allocation, the Preferred Stock have an effective conversion price of \$2.37 per common share, which was equal to the fair value of our common stock on the commitment date. Therefore, no BCF is present.

The warrants are exercisable at an exercise price of \$4.64 per share, subject to adjustments as provided under the terms of the warrants. The warrants are immediately exercisable and expire on December 31, 2019. We also entered into a registration rights agreement (Registration Rights Agreement) with certain of the Purchasers, excluding those Purchasers affiliated with our directors and officers, requiring us to register for the resale of the relevant securities. We registered all of the relevant securities issued in the Private Placement for resale on a Form S-3 filed with the SEC, as required under the Registration Rights Agreement, and the registration statement was declared effective on September 27, 2017.

We evaluated the warrants for liability or equity classification under ASC 815, *Derivative and Hedging* (ASC 815) and determined that equity treatment was appropriate because the warrants are indexed to our common stock and no cash settlement is required except for (i) liquidation of the Company, or (ii) a change in control in which the common stockholders also received cash.

Registration Statement on Form S-3

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 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. Shares underlying any awards under the 2014 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.

2015 Stock Plan

In April 2015, our board of directors adopted, and our stockholders approved, the 2015 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, 1,191,566, 949,793 and 946,803 additional shares were reserved for issuance under the 2015 Plan on January 1, 2018, 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 filed a registration statement on Form S-8 on March 22, 2017 to register the shares of common stock underlying this option. In addition, from time to time, we may make inducement grants of stock options to new employees. There were no inducement awards granted in 2017.

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, 297,891, 237,448 and 236,700 additional shares were reserved for issuance under the 2015 ESPP on January 1, 2018, 2017 and 2016, respectively.

Stock-based Compensation

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, 2016	4,014,988	\$ 6.73		
Granted	1,508,119	\$ 3.51		
Exercised	(75,289)	\$ 2.47		
Canceled/forfeited/expired	(830,759)	\$ 7.99		
Outstanding as of December 31, 2017	4,617,059	\$ 5.52	7.37	\$ 1,370
Options vested and expected to vest as of December 31, 2017	4,617,059	\$ 5.52	7.37	\$ 1,370
Options exercisable as of December 31, 2017	2,220,670	\$ 6.01	6.23	\$ 1,070

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,		
	2017	2016	2015
Expected term (in years)	5.50 – 6.08	5.50 – 6.08	5.50 – 6.08
Risk-free interest rate	1.9% – 2.1%	1.2% – 2.1%	1.5% – 1.9%
Expected volatility	99.1% – 124.4%	80.7% – 84.5%	79.2% – 100.9%
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:

	Years Ended December 31,		
	2017	2016	2015
Expected term (in years)	0.50	0.50	0.50
Risk-free interest rate	0.6% – 1.0%	0.4% – 0.6%	0.3%
Expected volatility	74.5% – 115.2%	75.5% – 80.8%	67.3%
Expected dividend yield	0.0%	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 to our executives, 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 market condition by October 2017, 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 market 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 vested. As of October 2017, the market condition for these performance options were not met and therefore were forfeited.

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 market conditions by January 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 vested. *Refer to Note 10, Subsequent Events for further discussion of these options.*

There were no performance options with a market condition granted during 2017.

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, 2017, 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, 2016	76,713	\$ 4.95
Granted	22,000	\$ 3.30
Released	(36,099)	\$ 4.96
Forfeited	(13,314)	\$ 4.67
Balance as of December 31, 2017	49,300	\$ 4.28

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,		
	2017	2016	2015
Research and development	\$ 1,399	\$ 1,876	\$ 2,524
General and administrative	5,385	3,153	2,332
	\$ 6,784	\$ 5,029	\$ 4,856

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, 2017, 2016 and 2015 was \$2.85, \$3.34 and \$11.29, respectively. The total fair value of restricted stock units vested during the years ended December 31, 2017, 2016 and 2015 was \$0.1 million, \$13,000 and none, respectively. The aggregate intrinsic value of stock options exercised during the years ended December 31, 2017, 2016 and 2015 was \$0.3 million, \$34,000 and \$1.9 million, respectively. As of December 31, 2017, total unrecognized share-based compensation expense related to unvested stock options and restricted stock units was approximately \$6.0 million. This unrecognized cost is expected to be recognized ratably over a weighted-average period of approximately 2.6 years.

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.

During the fourth quarter of 2017, in connection with the change of status of our then-Chief Executive Officer to an advisor consulting role, we modified certain terms of outstanding options granted to the executive. We recorded \$1.9 million of share-based compensation expense related to the modifications. We determined that vesting of the shares underlying the options will occur whether or not our then-Chief Executive Officer provides substantive service. In addition, in connection with the departure of our then-Chief Business Officer, we modified certain terms of outstanding options previously granted to the executive. As a result, we recorded \$0.3 million in share-based compensation expense related to the modification.

Warrants

Warrants outstanding as of December 31, 2017 is as follows:

Number Outstanding	Exercise Price Per Share	Expiration Date
6,488,205	\$ 4.64	December 2019
2,006	\$ 7.48	March 2021
14,913	\$ 20.12	July 2023
95,542	\$ 3.14	November 2023
41,666	\$ 3.60	June 2024
40,376	\$ 3.72	December 2024
<u>6,682,708</u>		

Common Stock Reserved for Future Issuance

Common stock reserved for future issuance is as follows:

	December 31,	
	2017	2016
Class X Preferred Stock (if-converted to common stock)	11,429,760	—
Common stock warrants	6,682,708	121,512
Common stock options and awards outstanding	4,666,359	4,091,701
Shares available under the 2015 Plan	765,427	510,760
Shares available under the 2015 ESPP	583,819	407,542
	<u>24,128,073</u>	<u>5,131,515</u>

7. Income Tax

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

	Years Ended December 31,		
	2017	2016	2015
United States	\$ (47,712)	\$ (57,096)	\$ (47,490)
Foreign	(495)	(808)	(483)
	<u>\$ (48,207)</u>	<u>\$ (57,904)</u>	<u>\$ (47,973)</u>

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,		
	2017	2016	2015
Expected income taxes benefit at federal statutory rate	\$ (16,390)	\$ (19,687)	\$ (16,311)
State income taxes, net of federal benefit	(13)	—	—
Permanent items and other	1,311	675	865
Research credits	(2,286)	(6,800)	(2,674)
Unrecognized tax benefits	914	2,720	1,070
Foreign rate differential	87	141	84
Change in tax rate	(25)	—	3,551
Tax cuts and Jobs Act	27,933	—	—
Change in valuation allowance	(11,531)	22,902	13,415
Income tax (benefit) expense	<u>\$ —</u>	<u>\$ (49)</u>	<u>\$ —</u>

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 \$59.7 million and \$71.1 million as of December 31, 2017 and 2016, 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,	
	2017	2016
Net operating loss carryforwards	\$ 27,226	\$ 33,713
Capitalized research and development expenses	16,218	21,624
Research credits and other state credits	11,229	9,227
Intangible assets	2,210	3,874
Reserve and accruals	2,843	2,711
Valuation allowance	(59,726)	(71,149)
Net deferred tax assets	<u>\$ —</u>	<u>\$ —</u>

As of December 31, 2017, we had approximately \$112.5 million, \$119.2 million, and \$7.0 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 2021, respectively. The foreign net operating losses carry over indefinitely. As of December 31, 2017, we had federal and state research and development credit carryforwards of approximately \$3.6 million and \$3.2 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 \$12.5 million of federal Orphan Drug Credits as of December 31, 2017, which will begin to expire in 2035.

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 analyses through December 31, 2017, and are in the process of analyzing the impact to our NOL and research and development tax credit carryforwards. Due to the existence of the valuation allowance, any

impact to the NOL and R&D tax credit carryforwards from Section 382 analysis will be offset by a corresponding adjustment to valuation allowance, resulting no tax provision impact. Ownership changes that may have occurred subsequent to December 31, 2017, 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, 2017, 2016 and 2015.

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,		
	2017	2016	2015
Balance as of beginning of year	\$ 13,000	\$ 5,033	\$ 1,106
Increase (decrease) related to prior year tax positions	(189)	1,890	2,404
Increase related to current year tax positions	3,747	6,077	1,523
Balance as of end of year	<u>\$ 16,558</u>	<u>\$ 13,000</u>	<u>\$ 5,033</u>

We do not anticipate that the amount of unrecognized tax benefits as of December 31, 2017 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.

The Tax Cuts and Jobs Act (the Act) was enacted on December 22, 2017. Among other changes, the Act reduces the U.S. federal corporate tax rate from 34 percent to 21 percent. In accordance with Staff Accounting Bulletin 118, as of December 31, 2017, we have not completed our accounting for the tax effects of enactment of the Act; however, in certain cases, as described below, we have made a reasonable estimate of the effects on our existing deferred tax balances. In all cases, we will continue to make and refine our calculations as additional analysis is completed. In addition, our estimate may also be effected as we gain a more thorough understanding of the tax law.

We remeasured certain deferred tax assets and liabilities based on the rates at which they are expected to reverse in the future, which is generally 21 percent. However, we are still analyzing certain aspects of the Act and refining our calculations, which could potentially affect the measurement of these balances or give rise to new deferred tax amounts. The provisional amount recorded related to the remeasurement of our deferred tax balance was \$27.9 million, which was fully offset by a decrease in our valuation allowance.

Due to uncertainties which currently exist in the interpretation of the provisions of the Act regarding Internal Revenue Code (IRC) Section 162(m), the Company is continuing to evaluate the potential impacts of IRC Section 162(m) as amended by the Act in its financial statements.

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, \$0.2 million and \$0.1 million during the years ended December 31, 2017, 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 2017 and 2016 are as follows (in thousands, except per share data):

	For the quarters ended			
	March 31	June 30	September 30	December 31
2017:				
Operating expenses	\$ 13,211	\$ 11,907	\$ 10,827	\$ 11,200
Net loss	(13,405)	(12,138)	(11,190)	(11,474)
Basic and diluted net loss per share	\$ (0.56)	\$ (0.51)	\$ (0.43)	(0.39)
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)

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

On January 4, 2018, the market condition for the performance options with market conditions granted in January 2016 was not met. As a result, 96,883 performance options, the outstanding performance options as of January 4, 2018, were forfeited.

In February 2018, we amended the agreement with TSRI to provide additional funding bringing the total to \$2.0 million for the preceding 12 months.

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, 2017.

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 15d-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, 2017, 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, 2017.

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, 2017, 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 2018 Annual Meeting of Stockholders within 120 days after the end of the fiscal year ended December 31, 2017, 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:*

	Page
Report of Independent Registered Public Accounting Firm	66
Consolidated Balance Sheets	67
Consolidated Statements of Operations	68
Consolidated Statements of Comprehensive Loss	69
Consolidated Statements of Stockholders' Equity (Deficit)	70
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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.

EXHIBIT INDEX

Exhibit Number	Exhibit Title	Form	Incorporated by File No.	Reference Exhibit	Filing Date
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
3.3	Certificate of Designation of Preferences, Rights and Limitations of Class X Convertible Preferred Stock	8-K	001-37378	3.1	August 31, 2017
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 March 18, 2011	S-1	333-203272	4.3	April 6, 2015
4.3	Warrant to Purchase Stock issued to Silicon Valley Bank on July 24, 2013	S-1	333-203272	4.4	April 6, 2015
4.4	Warrant to Purchase Stock issued to Silicon Valley Bank on November 18, 2016	10-K	001-37378	4.5	March 16, 2017
4.5	Warrant to Purchase Stock issued to Solar Capital Ltd on November 18, 2016	10-K	001-37378	4.6	March 16, 2017
4.6	Warrant to Purchase Stock issued to Silicon Valley Bank on June 30, 2017	10-Q	001-37378	4.7	August 14, 2017
4.7	Warrant to Purchase Stock issued to Solar Capital Ltd on June 30, 2017	10-Q	001-37378	4.8	August 14, 2017
4.8	Warrant to Purchase Stock issued to Silicon Valley Bank on December 22, 2017	—	—	—	Filed herewith
4.9	Warrant to Purchase Stock issued to Solar Capital Ltd on December 22, 2017	—	—	—	Filed herewith
4.10	Form of Warrant to Purchase Common Stock	8-K	001-37378	10.3	August 28, 2017
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 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
10.4	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
10.5	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, 2017	10-K	001-37378	10.8	March 16, 2017
10.6	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

Exhibit Number	Exhibit Title	Form	Incorporated by Reference File No.	Reference Exhibit	Filing Date
10.7	Form of Indemnification Agreement entered into between the Registrant and its directors	S-1/A	333-203272	10.12	April 27, 2015
10.8	Form of Indemnification Agreement entered into between the Registrant and its officers	S-1/A	333-203272	10.13	April 27, 2015
10.9#	2015 Employee Stock Purchase Plan	S-1/A	333-203272	10.14	April 27, 2015
10.10†	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
10.11#	Senior Executive Cash Incentive Bonus Plan	8-K	001-37378	10.1	January 29, 2016
10.12#	Executive Severance and Change in Control Policy	10-K	001-37378	10.16	March 30, 2016
10.13#	Registrant's Non-Qualified Stock Option Agreement for Non-Plan Inducement Grant	10-Q	001-37378	10.1	November 14, 2016
10.14†	Loan and Security Agreement by and between the Registrant and Silicon Valley Bank and Solar Capital Ltd, dated November 18, 2016	10-K	001-37378	10.17	March 16, 2017
10.15	Second Amendment to Lease between the Registrant and BMR-3545-3575 John Hopkins LP (as successor-in-interest to BMR-John Hopkins Court, LLC), dated April 27, 2017	10-Q	001-37378	10.1	May 11, 2017
10.16	First Amendment to Loan and Security Agreement between the Registrant and Silicon Valley Bank and Solar Capital Ltd, dated June 30, 2017	10-Q	001-37378	10.1	August 14, 2017
10.17	Securities Purchase Agreement, dated August 27, 2017, by and among the Company and the Purchasers	8-K	001-37378	10.1	August 28, 2017
10.18	Registration Rights Agreement, dated August 27, 2017, by and among the Company and the Purchasers	8-K	001-37378	10.2	August 28, 2017
10.19#	Employment Agreement, dated November 1, 2017, by and between the Company and Sanjay S. Shukla, M.D., M.S.	10-Q	001-37378	10.4	November 14, 2017
10.20#	Strategic Advisor Agreement, dated November 1, 2017, by and between the Company and John D. Mendlein, Ph.D.	10-Q	001-37378	10.5	November 14, 2017
10.21	Second Amendment to Loan and Security Agreement between the Registrant and Silicon Valley Bank and Solar Capital Ltd, dated October 10, 2017	—	—	—	Filed herewith
10.22	Transition and Separation Agreement between Registrant and Sanuj K. Ravindran dated December 11, 2017	—	—	—	Filed herewith
10.23	Third Amendment to Loan and Security Agreement between the Registrant and Silicon Valley Bank and Solar Capital Ltd, dated December 22, 2017	—	—	—	Filed herewith
14.1	Code of Business Conduct and Ethics	10-Q	001-37378	14.1	June 18, 2015

Exhibit Number	Exhibit Title	Form	Incorporated by Reference		Filing Date
			File No.	Exhibit	
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.

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 20, 2018

By /s/ Sanjay S. Shukla
 Sanjay S. Shukla, M.D., M.S.
 President, Chief Executive Officer and Director
(Principal Executive Officer)

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Sanjay S. Shukla 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
<u>/s/ Sanjay S. Shukla</u> Sanjay S. Shukla, M.D., M.S.	President, Chief Executive Officer and Director (Principal Executive Officer)	March 20, 2018
<u>/s/ John T. Blake</u> John T. Blake	Senior Vice President, Finance (Principal Financial and Accounting Officer)	March 20, 2018
<u>/s/ John K. Clarke</u> John K. Clarke	Chairman of the Board	March 20, 2018
<u>/s/ Srinivas Akkaraju</u> Srinivas Akkaraju, M.D., Ph.D.	Director	March 20, 2018
<u>/s/ James C. Blair</u> James C. Blair, Ph.D.	Director	March 20, 2018
<u>/s/ Timothy P. Coughlin</u> Timothy P. Coughlin	Director	March 20, 2018
<u>/s/ Jeffrey S. Hatfield</u> Jeffrey S. Hatfield.	Director	March 20, 2018
<u>/s/ John D. Mendlein</u> John D. Mendlein, Ph.D.	Director	March 20, 2018
<u>/s/ Amir H. Nashat</u> Amir H. Nashat, Sc.D.	Director	March 20, 2018
<u>/s/ Paul Schimmel</u> Paul Schimmel, Ph.D.	Director	March 20, 2018

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

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

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 Blake
Fax: (858) 875-1110
Email: jblake@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: Sr. Vice President, 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):

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

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 DECEMBER 22, 2017, 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 Blake
Fax: (858) 875-1110
Email: jblake@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: Sr. Vice President, Finance

“HOLDER”

SOLAR CAPTIAL 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):

**SECOND AMENDMENT TO
LOAN AND SECURITY AGREEMENT**

THIS **SECOND AMENDMENT** to Loan and Security Agreement (this "**Amendment**") is entered into as of October 10, 2017, by and between **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 of the Loan Agreement (as defined below) or otherwise party thereto from time to time (each a "**Lender**" and collectively, the "**Lenders**") 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 **ATYR PHARMA, INC.**, a Delaware corporation with offices located at 3545 John Hopkins Court, Suite 250, San Diego, CA 92121 ("**Borrower**").

Recitals

A. Collateral Agent, Lenders and Borrower have entered into that certain Loan and Security Agreement dated as of November 18, 2016 (as amended from time to time, including but not limited to that certain First Amendment to Loan and Security Agreement dated as of June 30, 2017, the "**Loan Agreement**").

B. Lenders have extended credit to Borrower for the purposes permitted in the Loan Agreement.

C. Borrower has requested that Collateral Agent and Lenders (i) modify the Change in Control Definition and (ii) make certain other revisions to the Loan Agreement as more fully set forth herein.

D. Collateral Agent and Lenders have agreed to modify such consent and to amend certain provisions of the Loan Agreement, but only to the extent, in accordance with the terms, subject to the conditions and in reliance upon the representations and warranties set forth below.

Agreement

Now, Therefore, in consideration of the foregoing recitals and other good and valuable consideration, the receipt and adequacy of which is hereby acknowledged, and intending to be legally bound, the parties hereto agree as follows:

1. Definitions. Capitalized terms used but not defined in this Amendment shall have the meanings given to them in the Loan Agreement.

2. Amendment to Loan Agreement.

2.1 Section 13.1 (Definitions). The following term and its definition hereby are amended and restated in their entirety, to Section 13.1 of the Loan Agreement as follows:

"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 forty-nine percent (49%) 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 directors 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.

3. Limitation of Amendment.

3.1 The amendment set forth in **Section 2** above is effective for the purposes set forth herein and shall be limited precisely as written and shall not be deemed to (a) be a consent to any amendment, waiver or modification of any other term or condition of any Loan Document, or (b) otherwise prejudice any right or remedy which Collateral Agent or any Lender may now have or may have in the future under or in connection with any Loan Document.

3.2 This Amendment shall be construed in connection with and as part of the Loan Documents and all terms, conditions, representations, warranties, covenants and agreements set forth in the Loan Documents, except as herein amended, are hereby ratified and confirmed and shall remain in full force and effect.

4. Representations and Warranties. To induce Collateral Agent and Lenders to enter into this Amendment, Borrower hereby represents and warrants to Collateral Agent and Lenders as follows:

4.1 Immediately after giving effect to this Amendment (a) the representations and warranties contained in the Loan Documents are true and correct in all material respects as of the date hereof (except to the extent such representations and warranties relate to an earlier date, in which case they are true and correct as of such date), and (b) no Event of Default has occurred and is continuing;

4.2 Borrower has the power and authority to execute and deliver this Amendment and to perform its obligations under the Loan Agreement, as amended by this Amendment;

4.3 The organizational documents of Borrower delivered to Collateral Agent and Lenders on the date hereof are true, accurate and complete and have not been amended, supplemented or restated and are and continue to be in full force and effect;

4.4 The execution and delivery by Borrower of this Amendment and the performance by Borrower of its obligations under the Loan Agreement, as amended by this Amendment, have been duly authorized;

4.5 The execution and delivery by Borrower of this Amendment and the performance by Borrower of its obligations under the Loan Agreement, as amended by this Amendment, do not and will not contravene (a) any material requirement of Law binding on or affecting Borrower, (b) any material agreement with a Person binding on Borrower, (c) any order, judgment or decree of any court or other governmental or public body or authority, or subdivision thereof, binding on Borrower, or (d) the organizational documents of Borrower;

4.6 The execution and delivery by Borrower of this Amendment and the performance by Borrower of its obligations under the Loan Agreement, as amended by this Amendment, do not require any order, consent, approval, license, authorization or validation of, or filing, recording or registration with, or exemption by any governmental or public body or authority, or subdivision thereof, binding on Borrower, (except as have been made and prior to the date hereof and are being obtained pursuant to Section 6.1(b) of the Loan Agreement or which the failure to obtain would not reasonably be expected to result in a Material Adverse Effect); and

4.7 This Amendment has been duly executed and delivered by Borrower and is the binding obligation of Borrower, enforceable against Borrower in accordance with its terms, except as such enforceability may be limited by bankruptcy, insolvency, reorganization, liquidation, moratorium or other similar laws of general application and equitable principles relating to or affecting creditors' rights.

5. Counterparts. This Amendment may be executed in any number of counterparts and all of such counterparts taken together shall be deemed to constitute one and the same instrument.

6. Effectiveness. This Amendment shall be deemed effective upon the due execution and delivery to Collateral Agent and Lenders of (i) this Amendment by each party hereto, and (ii) Borrower's payment of all Lenders' Expenses incurred through the date of this Amendment.

[Balance of Page Intentionally Left Blank]

In Witness Whereof, the parties hereto have caused this Amendment to be duly executed and delivered as of the date first written above.

COLLATERAL AGENT AND LENDER:

SILICON VALLEY BANK

By: /s/ Anthony Flores
Name: Anthony Flores
Title: Director

LENDER:

SOLAR CAPITAL LTD.

By: /s/ Neil J. Bonanno
Name: Neil J. Bonanno
Title: Authorized Signatory

BORROWER:

ATYR PHARMA, INC.

By: /s/ John T. Blake
Name: John T. Blake
Title: SVP, Finance

[Signature Page to First Amendment to Loan and Security Agreement]

December 11, 2017

PERSONAL AND CONFIDENTIAL

Sanuj K. Ravindran, M.D.
22 Harper Street
San Francisco, CA 94131

Re: Transition and Separation Agreement

Dear Sanuj:

As discussed, this Transition and Separation Agreement (the "Agreement") confirms your separation from employment with aTyr Pharma, Inc. (the "Company") effective as of December 31, 2017 (the "Separation Date").

Assuming that, as specified in Section 1 below, your employment ends on December 31, 2017 and not before that date due to your resignation or termination on or before that date for Cause (as defined under the Company's December 21, 2015 Executive Severance and Change in Control Policy (the "Severance Policy")), the Company will treat your separation from employment on December 31, 2017 as a termination without Cause not in connection with a Sale Event for purposes of the Severance Policy. Accordingly, this Agreement sets forth the severance agreement referenced in the Severance Policy, your execution and non-revocation of which is a condition of your right to receive the benefits described in Section 1 therein (the "Severance Benefits"). Further, because the Company would like to make your transition from employment as smooth as possible, this Agreement also offers you an extended exercise window for your vested equity (as described in Section 2(b) below) and the opportunity to be retained by the Company as a consultant pursuant to the terms of the Consulting Agreement (as defined in Section 2(c) below).

Regardless of whether you enter into this Agreement, the following shall occur:

- the Company will pay you your accrued salary through your last day of employment;
 - the Company will pay you your accrued but unused vacation through your last day of employment;
 - you will not be eligible for an annual bonus in 2017 given that you will not remain employed by the Company on the bonus payment date;
 - the Company will provide you with the right to continue group health care coverage after your last day of employment under the federal law known as "COBRA", which will be described in a separate written notice;
-

- the Company will reimburse you for any outstanding, reasonable business expenses that you have incurred on the Company's behalf through your last day of employment, after the Company's timely receipt of appropriate documentation pursuant to the Company's business expense reimbursement policy;
- you will remain bound by your continuing post-employment obligations under your January 8, 2016 Employee Nondisclosure and Assignment Agreement (the "**NDA**"), which include, without limitation, your obligations to not use or disclose the Company's Proprietary Information (as defined in the NDA), to immediately return all Company materials and Proprietary Information (unless the Company confirms in writing that you can keep any such materials and Proprietary Information to provide services pursuant to the Consulting Agreement), refrain from prohibited employee solicitation activities for a period of one (1) year after your last day of employment, and to refrain from disparaging activities; and
- you will cease vesting on your last day of employment in your outstanding stock options and other equity awards granted to you on January 4, 2016, September 13, 2016, and February 7, 2017 (collectively, the "**Equity Grants**") and, thereafter, (i) your right to exercise any vested portion of the Equity Grants (after accounting for any applicable accelerated vesting described in Section 1 of the Severance Policy if this Agreement becomes effective) shall be governed by the applicable grant agreements and the Company's 2015 Stock Option and Grant Plan (collectively, the "**Equity Documents**") as amended by Section 2(b) below (if applicable) and (ii) any unvested portion (after accounting for any applicable accelerated vesting described in Section 1 of the Severance Policy if this Agreement becomes effective) shall lapse and not be exercisable by you.¹

You and the Company agree that neither the Company tendering this Agreement to you nor it taking effect shall constitute Good Reason under the Severance Policy.

The remainder of this letter sets forth the terms of the Agreement. You acknowledge that you are entering into this Agreement knowingly and voluntarily. With those understandings, you and the Company agree as follows:

1. Separation from Employment

Unless you sooner resign or are terminated by the Company for Cause, your at-will employment with the Company will terminate on December 31, 2017 and such termination shall be treated as

¹ For the avoidance of doubt, below is a summary of the vested/unvested portions of the Equity Grants as of the Separation Date and before accounting for any applicable accelerated vesting described in Section 1 of the Severance Policy:

January 4, 2016 grant (time-based vesting): 73,313 shares vested, 79,687 shares unvested.

January 4, 2016 Equity grant (performance-based vesting): 0 shares vested, 10,750 shares unvested.

September 13, 2016 grant (time-based vesting): 14,219 shares vested, 31,281 shares unvested.

February 7, 2017 grant (time-based vesting): 8,333 shares vested, 31,667 shares unvested.

a termination without Cause for purposes of the Severance Policy. For purposes of this Agreement, the *actual* last day of your employment with the Company—whether December 31, 2017 or an earlier date due to your resignation or termination for Cause—shall be referred to as the “Separation Date,” and the period from the date of this Agreement through the Separation Date shall be referred to as the “Transition Period.”

During the Transition Period, as an at-will employee you will continue to (i) receive your current base salary; (ii) be eligible to participate in the Company’s employee benefit plans subject to the terms and conditions of such plans; and (iii) vest in any outstanding equity grants pursuant to the terms of the Equity Documents.

For your part, during the Transition Period, you will perform, on a full-time basis, the duties of your positions and any transitional duties requested by the Company (the “Transitional Duties”). You shall perform the Transitional Duties from the Company’s offices unless directed by the Company to perform them from home or another business location.

You agree to sign any documentation reasonably requested by the Company to effectuate your separation from employment from any positions you hold with the Company. If you apply for unemployment compensation benefits under state law, the Company shall not dispute your eligibility for such benefits. This shall not affect the Company’s obligation to respond truthfully to governmental agency requests for information related to unemployment compensation eligibility.

2. Severance Benefits, Extended Exercise Window, and Consulting Agreement

Provided that this Agreement becomes effective, your employment terminates on December 31, 2017 without Cause as described in Section 1 above, you comply with this Agreement and your continuing obligations under the NDA, then the Company will provide you with the following:

(a) Severance Benefits. The Company will provide you with the Severance Benefits pursuant to the terms of the Severance Policy. The cash payment portions of the Severance Benefits shall be subject to applicable tax-related deductions and withholdings and shall commence within 60 days following the Separation Date. With respect to the accelerated vesting portion of the Severance Benefits, if the Separation Date occurs after the Effective Date (defined in Section 8(i) below), then the accelerated vesting will occur on the Separation Date.² Alternatively, if the Effective Date occurs after the Separation Date, then any termination or forfeiture of the unvested portion of the Equity Grants that would otherwise occur under the Equity Documents on the Separation Date in the absence of this Agreement (and its accelerated vesting benefit) becoming effective (x) will be delayed until the Effective Date and (y) will only occur if

² For clarification purposes, below is a summary of the portions of the Equity Grants that would be vested/unvested after accounting for the accelerated vesting described in Section 1 of the Severance Policy and this Section 2(a):

January 4, 2016 grant (time-based vesting): 111,563 shares vested, 41,437 shares unvested.

January 4, 2016 Equity grant (performance-based vesting): 0 shares vested, 10,750 shares unvested.

September 13, 2016 grant (time-based vesting): 25,594 shares vested, 19,906 shares unvested.

February 7, 2017 grant (time-based vesting): 18,333 shares vested, 21,667 shares unvested

this Agreement does not become effective. You acknowledge and agree that upon your receipt of the Severance Benefits, you will have no further rights under the Severance Policy.

(b) Extension of Exercise Window. If the Consulting Agreement becomes effective, then on the later of December 31, 2017 or the Effective Date, the exercise window under the Equity Documents for any vested portion of the Equity Grants (after accounting for any applicable accelerated vesting described in Section 1 of the Severance Policy if this Agreement becomes effective) shall be extended until the three (3) month anniversary of the termination of the Consulting Agreement.

(c) Consulting Agreement. The Company hereby offers you the opportunity to be retained as a consultant pursuant to the terms of the Consulting Agreement attached hereto as Exhibit A. To accept this offer, you must sign and return the Consulting Agreement at the same time you sign and return this Agreement. For the avoidance of doubt, the Consulting Agreement will not become effective until the later of December 31, 2017 or the Effective Date, and if this Agreement does not become effective then the Consulting Agreement shall be null and void.

3. Release of Claims

In consideration for, among other terms, the Severance Benefits, the extended exercise window, and the offer of the Consulting Agreement, to which you acknowledge you would otherwise not be entitled, you voluntarily release and forever discharge the Company, its affiliated and related entities, its and their respective predecessors, successors and assigns, its and their respective employee benefit plans and fiduciaries of such plans, and the current and former officers, directors, shareholders, employees, attorneys, accountants and agents of each of the foregoing in their official and personal capacities (collectively referred to as the "Releasees") generally from all claims, demands, debts, damages and liabilities of every name and nature, known or unknown ("Claims") that, as of the date when you sign this Agreement, you have, ever had, now claim to have or ever claimed to have had against any or all of the Releasees. This release includes, without limitation, all Claims: relating to your employment by the Company and the decision regarding your separation from employment with the Company; of wrongful discharge or violation of public policy; of breach of contract; of defamation or other torts; of retaliation or discrimination under federal, state or local law (including, without limitation, Claims of discrimination or retaliation under the Age Discrimination in Employment Act, the Americans with Disabilities Act, Title VII of the Civil Rights Act of 1964, and the California Fair Employment and Housing Act); under any other federal or state statute (including, without limitation, Claims under the Fair Labor Standards Act, the Family and Medical Leave Act, the California Family Rights Act and any other state or local leave of absence law); for wages, bonuses, incentive compensation, commissions, stock, stock options, vacation pay or any other compensation or benefits, either under the California Labor Code or otherwise; and for damages or other remedies of any sort, including, without limitation, compensatory damages, punitive damages, injunctive relief and attorney's fees; *provided*, however, that this release shall not affect your rights under this Agreement or rights that cannot be released as a matter of law.

You agree not to accept damages of any nature, other equitable or legal remedies for your own benefit or attorney's fees or costs from any of the Releasees with respect to any Claim released by

this Agreement. As a material inducement to the Company to enter into this Agreement, you represent that you have not assigned any Claim to any third party.

4. California Civil Code Section 1542

You acknowledge that you have been advised to consult with legal counsel and are familiar with the provisions of California Civil Code Section 1542, a statute that otherwise prohibits the release of unknown claims, which provides as follows:

A GENERAL RELEASE DOES NOT EXTEND TO CLAIMS WHICH THE CREDITOR DOES NOT KNOW OR SUSPECT TO EXIST IN HIS OR HER FAVOR AT THE TIME OF EXECUTING THE RELEASE, WHICH IF KNOWN BY HIM OR HER MUST HAVE MATERIALLY AFFECTED HIS OR HER SETTLEMENT WITH THE DEBTOR.

You, being aware of said code section, agree to expressly waive any rights you may have thereunder, as well as under any other statute or common law principles of similar effect.

5. Continuing Obligations under the NDA

Regardless of whether you execute this Agreement, you will remain bound by your continuing obligations under the NDA, the terms of which are incorporated herein by reference. For the avoidance of doubt, such continuing obligations include, without limitation, your obligations to not use or disclose the Company's Proprietary Information (as defined in the NDA), to immediately return all Company materials and Proprietary Information (unless the Company confirms in writing that you can keep any such materials and Proprietary Information to provide services pursuant to the Consulting Agreement), refrain from prohibited employee solicitation activities for a period of one (1) year after the Separation Date, and to refrain from disparaging activities.

6. Confidentiality of Agreement-Related Information

You agree, to the fullest extent permitted by law, to keep all Agreement-Related Information completely confidential. "Agreement-Related Information" means the existence and terms of this Agreement. Notwithstanding the foregoing, you may disclose Agreement-Related Information to your immediate family members and any legal or tax advisors, and to them only provided that they first agree for the benefit of the Company to keep Agreement-Related Information confidential. Nothing in this section shall be construed to prevent you from disclosing Agreement-Related Information to the extent required by a lawfully issued subpoena or duly issued court order; *provided* that you provide the Company with advance written notice and a reasonable opportunity to contest such subpoena or court order.

7. Future Cooperation

You agree to cooperate reasonably with the Company (including its outside counsel) in connection with (i) the contemplation, prosecution and defense of all phases of existing, past and future litigation about which the Company believes you may have knowledge or information; and (ii) responding to requests for information from regulatory agencies or other governmental authorities

(together “Cooperation Services”). You further agree to make yourself available to provide Cooperation Services at mutually convenient times during and outside of regular business hours as reasonably deemed necessary by the Company’s counsel. The Company shall not utilize this section to require you to make yourself available to an extent that would unreasonably interfere with subsequent full-time employment responsibilities that you may have. Cooperation Services include, without limitation, appearing without the necessity of a subpoena to testify truthfully in any legal proceedings in which the Company calls you as a witness. The Company shall reimburse you for any reasonable travel expenses that you incur due to your performance of Cooperation Services, after receipt of appropriate documentation consistent with the Company’s business expense reimbursement policy.

8. Other Provisions

(a) Termination of Payments. If you breach any of your obligations under this Agreement or the NDA, in addition to any other legal or equitable remedies it may have for such breach, shall have the right to terminate the Severance Benefits, terminate the extended exercise window, and/or terminate the Consulting Agreement. Such termination(s) in the event of your breach will not affect your continuing obligations under this Agreement, the NDA and the Consulting Agreement.

(b) Protected Disclosures and Other Protected Actions. Nothing contained in this Agreement limits your ability to file a charge or complaint with any federal, state or local governmental agency or commission (a “Government Agency”). In addition, nothing contained in this Agreement limits your ability to communicate with any Government Agency or otherwise participate in any investigation or proceeding that may be conducted by any Government Agency, including your ability to provide documents or other information, without notice to the Company, nor does anything contained in this Agreement apply to truthful testimony in litigation. If you file any charge or complaint with any Government Agency and if the Government Agency pursues any claim on your behalf, or if any other third party pursues any claim on your behalf, you waive any right to monetary or other individualized relief (either individually, or as part of any collective or class action); *provided* that nothing in this Agreement limits any right you may have to receive a whistleblower award or bounty for information provided to the Securities and Exchange Commission.

(c) Absence of Reliance. In signing this Agreement, you are not relying upon any promises or representations made by anyone at or on behalf of the Company.

(d) Enforceability. If any portion or provision of this Agreement (including, without limitation, any portion or provision of any section of this Agreement) shall to any extent be declared illegal or unenforceable by a court of competent jurisdiction, then the remainder of this Agreement, or the application of such portion or provision in circumstances other than those as to which it is so declared illegal or unenforceable, shall not be affected thereby, and each portion and provision of this Agreement shall be valid and enforceable to the fullest extent permitted by law.

(e) Waiver. No waiver of any provision of this Agreement shall be effective unless made in writing and signed by the waiving party. The failure of a party to require the performance of any term or obligation of this Agreement, or the waiver by a party of any breach of this

Agreement, shall not prevent any subsequent enforcement of such term or obligation or be deemed a waiver of any subsequent breach.

(f) Jurisdiction. You and the Company hereby agree that the state and federal courts nearest San Diego, California shall have the exclusive jurisdiction to consider any matters related to this Agreement, including without limitation any claim of a violation of this Agreement. With respect to any such court action, you submit to the jurisdiction of such courts and you acknowledge that venue in such courts is proper.

(g) Governing Law; Interpretation. This Agreement shall be interpreted and enforced under the laws of the State of California, without regard to conflict of law principles. In the event of any dispute, this Agreement is intended by the parties to be construed as a whole, to be interpreted in accordance with its fair meaning, and not to be construed strictly for or against either you or the Company or the “drafter” of all or any portion of this Agreement.

(h) Entire Agreement. This Agreement constitutes the entire agreement between you and the Company. This Agreement supersedes any previous agreements or understandings between you and the Company, except the NDA, Equity Documents (as amended by Sections 2(a)-(b) above (if applicable)), the Consulting Agreement, and any obligations specifically preserved in this Agreement.

(i) Time for Consideration; Effective Date. You understand and acknowledge that you have been given the opportunity to consider this Agreement for twenty-one (21) days from your receipt of this Agreement before signing it (the “Consideration Period”). In signing this Agreement, you acknowledge that you have knowingly and voluntarily entered into this Agreement. To accept this Agreement, you must return a signed original or a signed PDF copy of this Agreement so that it is received by Holly Chrzanowski Winter (3545 John Hopkins Court, Suite #250, San Diego, CA 92121; hchrzanowski@atyrpharma.com) at or before the expiration of the Consideration Period. If you sign this Agreement before the end of the Consideration Period, you acknowledge by signing this Agreement that such decision was entirely voluntary and that you had the opportunity to consider this Agreement for the entire Consideration Period. For the period of seven (7) days from the date when you sign this Agreement, you have the right to revoke this Agreement by written notice to Ms. Chrzanowski Winter. For such a revocation to be effective, it must be delivered so that it is received by Ms. Chrzanowski Winter at or before the expiration of the seven (7) day revocation period. This Agreement shall not become effective or enforceable during the revocation period. This Agreement shall become effective on the first business day following the expiration of the revocation period (the “Effective Date”).

(j) Counterparts. This Agreement may be executed in separate counterparts. When all counterparts are signed, they shall be treated together as one and the same document.

[signature page follows]

Please indicate your agreement to the terms of this Agreement by signing and returning a PDF copy within the time period and in the manner specified above.

Very truly yours,

ATYR PHARMA, INC.

/s/ Nancy Denyes Krueger

2017

Nancy Denyes Krueger
Vice President, Legal Affairs and Secretary

December 11,

Date

Enclosure: Exhibit A (Consulting Agreement)

You are advised to consult with an attorney before signing this Agreement. This is a legal document. Your signature will commit you to its terms. By signing below, you acknowledge that you have carefully read and fully understand all of the provisions of this Agreement and that you are knowingly and voluntarily entering into this Agreement.

/s/ Sanuj K. Ravindran

2017

Sanuj K. Ravindran, M.D.

December 11,

Date

EXHIBIT A TO TRANSITION AND SEPARATION AGREEMENT

CONSULTING AGREEMENT

This Consulting Agreement (“**Agreement**”) is made by and between aTyr Pharma, Inc. (“**Company**”), having a principal place of business at 3545 John Hopkins Court, Suite #250, San Diego, California 92121, and Sanuj K. Ravindran, M.D. (“**Consultant**”), an individual having a principal place of business at 22 Harper Street, San Francisco, CA 94131. This Agreement shall commence as of the later of the Effective Date or the Separation Date (as such terms are defined in the Transition and Separation Agreement to which this Agreement is attached) (the applicable date being the (“**Commencement Date**”).

1. **Retention of Services.** Company hereby retains Consultant to advise and consult with the Company in the communication and transition of information and knowledge relating to the Company’s business, including advisory services and support related to the Company’s business development efforts and investor relations plans.

2. **Compensation and Other Benefits.**

2.1 **Fees.** The Company will pay Consultant fees for services rendered at rates below, which will be paid in arrears within thirty (30) days after the end of the applicable month:

- For the first four (4) month period of the term of the Agreement: \$15,000 per month
- For the second four (4) month period of the term of the Agreement: \$10,000 per month
- For the third four (4) month period of the term of the Agreement: \$5,000 per month

For the avoidance of doubt, if the term of this Agreement terminates prior to December 31, 2018, Consultant will be entitled to receive only the fees through the month of termination (pro-rated in the month of termination based on when such termination occurs).

2.2 **Expenses.** Company shall reimburse Consultant for reasonable expenses incurred in connection with Consultant’s performance of services under this Agreement, provided that the expenses are approved in advance by the Chief Executive Officer of Company and Consultant promptly provides documentation satisfactory to Company to support Consultant’s request for reimbursement.

3. **Independent Contractor Relationship.** Consultant’s relationship with Company will be that of an independent contractor, and nothing in this Agreement is intended to, or should be construed to, create a partnership, agency, joint venture or employment relationship. Consultant will not be entitled to any of the benefits that Company may make available to its employees, including, but not limited to, group health, life insurance, profit-sharing or retirement benefits, paid vacation, holidays or sick leave. Consultant will not be authorized to make any representation, contract or commitment on behalf of Company unless specifically requested or authorized in

writing to do so by the Chief Executive Officer of Company. Consultant will be solely responsible for obtaining any business or similar licenses required by any federal, state or local authority. In addition, Consultant will be solely responsible for, and will file on a timely basis, all tax returns and payments required to be filed with, or made to, any federal, state or local tax authority with respect to the performance of services and receipt of fees under this Agreement. No part of Consultant's compensation will be subject to withholding by Company for the payment of any social security, federal, state or any other employee payroll taxes. Company will regularly report amounts paid to Consultant by filing a Form 1099-MISC with the Internal Revenue Service as required by law.

3.1 Method of Performing Services; Results. In accordance with Company's objectives, Consultant will determine the method, details and means of performing the services required by this Agreement. Company shall have no right to, and shall not, control the manner or determine the method of performing Consultant's services. Consultant shall provide the services for which Consultant is engaged to the reasonable satisfaction of Company. Company may suggest to Consultant, from time to time, methods or strategies Company believes may assist Consultant in the performance of Consultant's services under this Agreement. Consistent with Consultant's independent contractor status, however, Consultant shall exercise Consultant's independent business discretion in determining whether or not to follow Company's suggestions.

3.2 Workplace, Hours and Instrumentalities. Consultant may perform the services required by this Agreement at any place or location and at such times as Consultant shall determine. Consultant agrees to provide all tools and instrumentalities, if any, required to perform the services under this Agreement; however, Company will/may at its convenience make available to Consultant suitable office space, computer equipment, and the like, to facilitate the efficient rendering of Consultant's services to Company. Such facilities shall be used by Consultant, if at all, at Consultant's discretion.

4. Intellectual Property Rights.

4.1 Disclosure and Assignment of Innovations.

(a) Innovations; Company Innovations. "**Innovations**" includes processes, machines, compositions of matter, improvements, inventions (whether or not protectable under patent laws), works of authorship, information fixed in any tangible medium of expression (whether or not protectable under copyright laws), moral rights, mask works, trademarks, trade names, trade dress, trade secrets, know-how, ideas (whether or not protectable under trade secret laws), and all other subject matter protectable under patent, copyright, moral right, mask work, trademark, trade secret or other laws, and includes without limitation all new or useful art, combinations, discoveries, formulae, manufacturing techniques, technical developments, discoveries, artwork, software, and designs. "**Company Innovations**" are Innovations that Consultant, solely or jointly with others, conceives, reduces to practice, creates, derives, develops or makes within the scope of Consultant's work for Company under this Agreement.

(b) Disclosure and Ownership of Company Innovations. Consultant agrees to make and maintain adequate and current records of all Company Innovations, which

records shall be and remain the property of Company. Consultant agrees to promptly disclose to Company every Company Innovation. Consultant hereby does and will assign to Company, or Company's designee, Consultant's entire worldwide right, title and interest in and to all Company Innovations and all associated records and intellectual property rights.

(c) Assistance. Consultant agrees to execute upon Company's request a signed transfer of Company Innovations to Company for each of the Company Innovations, including, but not limited to, computer programs, notes, sketches, drawings and reports. Consultant agrees to assist Company in any reasonable manner to obtain, perfect and enforce, for Company's benefit, Company's rights, title and interest in any and all countries, in and to all patents, copyrights, moral rights, mask works, trade secrets, and other property rights in each of the Company Innovations. Consultant agrees to execute, when requested, for each of the Company Innovations (including derivative works, improvements, renewals, extensions, continuations, divisionals, continuations in part, or continuing patent applications thereof), (i) patent, copyright, mask work or similar applications related to such Company Innovation, (ii) documentation (including without limitation assignments) to permit Company to obtain, perfect and enforce Company's right, title and interest in and to such Company Innovation, and (iii) any other lawful documents deemed necessary by Company to carry out the purpose of this Agreement. If called upon to render assistance under this paragraph, Consultant will be entitled to a fair and reasonable fee in addition to reimbursement of authorized expenses incurred at the prior written request of Company. In the event that Company is unable for any reason to secure Consultant's signature to any document Consultant is required to execute under this Paragraph 4.1(c) ("**Assistance**"), Consultant hereby irrevocably designates and appoints Company and Company's duly authorized officers and agents as Consultant's agents and attorneys-in-fact to act for and in Consultant's behalf and instead of Consultant, to execute such document with the same legal force and effect as if executed by Consultant.

(d) Out-of-Scope Innovations. If Consultant incorporates any Innovations relating in any way to Company's business or demonstrably anticipated research or development or business which were conceived, reduced to practice, created, derived, developed or made by Consultant either outside of the scope of Consultant's work for Company under this Agreement or prior to the Commencement Date (collectively, the "**Out-of-Scope Innovations**") into any of the Company Innovations, Consultant hereby grants to Company or Company's designees a royalty-free, irrevocable, worldwide, fully paid-up license (with rights to sublicense through multiple tiers of sublicensees) to practice all applicable patent, copyright, moral right, mask work, trade secret and other intellectual property rights relating to any Out-of-Scope Innovations which Consultant incorporates, or permits to be incorporated, in any Company Innovations. Consultant agrees that Consultant will not incorporate, or permit to be incorporated, any Innovations conceived, reduced to practice, created, derived, developed or made by others or any Out-of-Scope Innovations into any of the Company Innovations without Company's prior written consent.

4.2 Confidential Information.

(a) Definition of Confidential Information. "**Confidential Information**" as used in this Agreement shall mean any and all technical and non-technical information including patent, copyright, trade secret, and proprietary information, techniques,

sketches, drawings, models, inventions, know-how, processes, apparatus, equipment, algorithms, software programs, software source documents, and formulae related to the current, future and proposed products and services of Company, Company's suppliers and customers, and includes, without limitation, Company Innovations, Company Property (defined below), and Company's information concerning research, experimental work, development, design details and specifications, engineering, financial information, procurement requirements, purchasing manufacturing, customer lists, business forecasts, sales and merchandising and marketing plans and information.

(b) Nondisclosure and Nonuse Obligations. Except as permitted in this paragraph, Consultant shall neither use nor disclose the Confidential Information. Consultant may use the Confidential Information solely to perform services for the benefit of Company. Consultant agrees that Consultant shall treat all Confidential Information of Company with the same degree of care as Consultant accords to Consultant's own Confidential Information, but in no case less than reasonable care. If Consultant is not an individual, Consultant agrees that Consultant shall disclose Confidential Information only to those of Consultant's employees who need to know such information, and Consultant certifies that such employees have previously agreed, either as a condition of employment or in order to obtain the Confidential Information, to be bound by terms and conditions substantially similar to those terms and conditions applicable to Consultant under this Agreement. Consultant agrees not to communicate any information to Company in violation of the proprietary rights of any third party. Consultant will immediately give notice to Company of any unauthorized use or disclosure of the Confidential Information and agrees to assist Company in remedying any such unauthorized use or disclosure of the Confidential Information.

(c) Exclusions from Nondisclosure and Nonuse Obligations. Consultant's obligations under Paragraph 4.2(b) ("Nondisclosure and Nonuse Obligations") with respect to any portion of the Confidential Information shall not apply to any such portion which Consultant can demonstrate: (a) was in the public domain at or subsequent to the time such portion was communicated to Consultant by Company through no fault of Consultant; (b) was rightfully in Consultant's possession free of any obligation of confidence at or subsequent to the time such portion was communicated to Consultant by Company; or (c) was developed by employees of Consultant independently of and without reference to any information communicated to Consultant by Company. A disclosure of Confidential Information by Consultant, either: (a) in response to a valid order by a court or other governmental body; (b) otherwise required by law; or (c) necessary to establish the rights of either party under this Agreement, shall not be considered to be a breach of this Agreement or a waiver of confidentiality for other purposes; provided, however, that Consultant shall provide prompt prior written notice thereof to Company to enable Company to seek a protective order or otherwise prevent such disclosure.

(d) Insider Trading. Consultant hereby acknowledges that Confidential Information disclosed by Company under this Agreement or obtained by Consultant in the course of performing duties hereunder may constitute material, non-public information with respect to Company under applicable securities laws. Consultant agrees to abide by all applicable securities laws with respect to such Confidential Information and, without limiting the generality of the foregoing or any other provision of this Agreement, agrees NOT to: (a) purchase or sell, directly or indirectly, any Company securities while in possession of relevant material, nonpublic

information relating to Company received from the Company or others in connection herewith; or (b) communicate any material, nonpublic information relating to Company to any other person in which it is reasonably foreseeable that such person is likely to (i) purchase or sell Company securities, or (ii) otherwise directly or indirectly benefit from such information. Without limiting any of the confidentiality and insider trading obligations included in this Agreement, Consultant shall not discuss any information concerning Company obtained by Consultant in the course of performing the Services with any financial, securities or industry analyst or with the media without the written agreement of Company.

(e) Defend Trade Secrets Act. Consultant acknowledges receipt of the following notice under 18 U.S.C § 1833(b)(1): “An individual shall not be held criminally or civilly liable under any Federal or State trade secret law for the disclosure of a trade secret that (A) is made (i) in confidence to a Federal, State, or local government official, either directly or indirectly, or to an attorney; and (ii) solely for the purpose of reporting or investigating a suspected violation of law; or (B) is made in a complaint or other document filed in a lawsuit or other proceeding, if such filing is made under seal.”

4.3 Ownership and Return of Company Property. All materials (including, without limitation, documents, drawings, models, apparatus, sketches, designs, lists, all other tangible media of expression), equipment, documents, data, and other property furnished to Consultant by Company, whether delivered to Consultant by Company or made by Consultant in the performance of services under this Agreement (collectively, the “**Company Property**”) are the sole and exclusive property of Company or Company’s suppliers or customers, and Consultant hereby does and will assign to Company all rights, title and interest Consultant may have or acquire in the Company Property. Consultant agrees to keep all Company Property at Consultant’s premises unless otherwise permitted in writing by Company. At the end of this Agreement, or at Company’s request, and no later than five (5) days after the end of this Agreement or Company’s request, Consultant shall destroy or deliver to Company, at Company’s option: (a) all Company Property; (b) all tangible media of expression in Consultant’s possession or control which incorporate or in which are fixed any Confidential Information; and (c) written certification of Consultant’s compliance with Consultant’s obligations under this subparagraph.

4.4 Observance of Company Rules. At all times while on Company’s premises, Consultant will observe Company’s rules and regulations with respect to conduct, health and safety and protection of persons and property.

5. No Conflict of Interest. During the term of this Agreement, Consultant will not accept work, enter into a contract, or accept an obligation, inconsistent or incompatible with Consultant’s obligations, or the scope of services rendered for Company, under this Agreement. Consultant warrants that, to the best of Consultant’s knowledge, there is no other contract or duty on the part of Consultant that conflicts with or is inconsistent with this Agreement. This paragraph 5 does not prevent Consultant from performing the same or similar services for clients other than Company so long as such services do not directly or indirectly conflict with Consultant’s obligations under this Agreement.

6. **Term and Termination.**

6.1 **Term.** This Agreement is effective as of the Commencement Date set forth above and will end December 31, 2018 unless sooner terminated in accordance with subparagraphs 6.2 or 6.3 below. This Agreement is renewable upon the mutual consent of both parties. The terms of such renewal must be in writing and signed by both Company and Consultant.

6.2 **Termination by Company.** Company may terminate this Agreement immediately upon Consultant's breach of this Agreement, the Employee Nondisclosure and Assignment Agreement dated January 8, 2016, or the Transition and Separation Agreement to which this Agreement is attached.

6.3 **Termination by Consultant.** Consultant may terminate this Agreement at any time, with termination effective thirty (30) days after Consultant's delivery to Company of written notice of termination.

6.4 **Duties Upon Termination.** Upon termination of this Agreement for any reason, Consultant agrees to cease all work on behalf of Company and promptly deliver the results to Company. Company shall promptly pay Consultant all fees and approved expenses incurred by Consultant to the date of termination within thirty (30) days after receiving Consultant's final invoice.

7. **General Provisions.**

7.1 **Successors and Assigns.** The rights and obligations of Company under this Agreement shall inure to the benefit of and shall be binding upon the successors and assigns of Company. Consultant may not assign its rights, subcontract or otherwise delegate its obligations under this Agreement without Company's prior written consent.

7.2 **Consultant Indemnification.** Consultant shall be liable for, and agrees to pay, any and all debts, claims, demands, liabilities, expenses, losses, injuries, damages and reasonable attorneys' fees arising out of Consultant's gross negligence in performing the services described in this Agreement. Further, Consultant shall indemnify and hold Company harmless from and against any and all debts, claims, demands, liabilities, expenses, losses, injuries, damages for injury to or death of persons, including, but not limited to, Consultant's employees, if any, and customers and employees of Company, and damages or destruction to property, including, but not limited to, property of Company, resulting, in any manner, from Consultant's gross negligence in performing the services described in this Agreement.

7.3 **Agreement to Arbitrate.** Consultant and Company agree to arbitrate any controversy, claim or dispute between them arising out of or in any way related to this Agreement, the consulting relationship between Consultant and Company, and any disputes upon termination of the consulting relationship, including claims for violation of any local, state or federal law, statute, regulation or ordinance or common law. The arbitration will be conducted in San Diego County, California, by a single neutral arbitrator and in accordance with the American Arbitration Association's ("AAA") then current rules for resolution of commercial disputes. The arbitrator shall have the power to enter any award that could be entered by a judge of the trial court of the

State of California, and only such power, and shall follow the law. In the event the arbitrator does not follow the law, the arbitrator will have exceeded the scope of his or her authority and the parties may, at their option, file a motion to vacate the award in court. The parties agree to abide by and perform any award rendered by the arbitrator. Judgment on the award may be entered in any court having jurisdiction thereof.

7.4 Survival. The definitions contained in this Agreement and the rights and obligations contained in Paragraphs 4 (“Intellectual Property Rights”) and 7 (“General Provisions”) will survive any termination or expiration of this Agreement.

7.5 Notices. Any notice required or permitted by this Agreement shall be in writing and shall be delivered as follows, with notice deemed given as indicated: (a) by personal delivery, when delivered personally; (b) by overnight courier, upon written verification of receipt; (c) by telecopy or facsimile transmission, upon acknowledgment of receipt of electronic transmission; or (d) by certified or registered mail, return receipt requested, upon verification of receipt. Notice shall be sent to the addresses set forth above or to such other address as either party may specify in writing.

7.6 Governing Law. This Agreement shall be governed in all respects by the laws of the United States of America and by the laws of the State of California, as such laws are applied to agreements entered into and to be performed entirely within California between California residents. Except for the matters to be resolved pursuant to subparagraph 7.3 hereof, each of the parties irrevocably consents to the personal jurisdiction of the federal and state courts located in California, as applicable, for any matter arising out of or relating to this Agreement, except that in actions seeking to enforce any order or any judgment of such federal or state courts located in California, such personal jurisdiction shall be nonexclusive.

7.7 Severability. If any provision of this Agreement is held by a court of law to be illegal, invalid or unenforceable, (i) that provision shall be deemed amended to achieve as nearly as possible the same economic effect as the original provision, and (ii) the legality, validity and enforceability of the remaining provisions of this Agreement shall not be affected or impaired thereby.

7.8 Waiver; Amendment; Modification. No term or provision hereof will be considered waived by Company, and no breach excused by Company, unless such waiver or consent is in writing signed by Company. The waiver by Company of, or consent by Company to, a breach of any provision of this Agreement by Consultant, shall not operate or be construed as a waiver of, consent to, or excuse of any other or subsequent breach by Consultant. This Agreement may be amended or modified only by mutual agreement of authorized representatives of the parties in writing.

7.9 Injunctive Relief for Breach. Consultant’s obligations under this Agreement are of a unique character that gives them particular value. Consultant’s breach of any of such obligations will result in irreparable and continuing damage to Company for which there will be no adequate remedy at law. Accordingly, in the event of such breach, the parties agree that Company will be entitled to injunctive relief and/or a decree for specific performance, and such other and further relief as may be proper (including monetary damages if appropriate).

7.10 Entire Agreement. This Agreement constitutes the entire agreement between the parties relating to this subject matter and supersedes all prior or contemporaneous oral or written agreements concerning such subject matter. The terms of this Agreement will govern all services undertaken by Consultant for Company.

[signature page follows]

Ex. A - 8

IN WITNESS WHEREOF, the parties have executed this Agreement as of the Commencement Date.

ATYR PHARMA, INC.

CONSULTANT

By: /s/ Nancy Denyes Krueger
Nancy Denyes Krueger
VP, Legal Affairs and Secretary

By: /s/ Sanuj K. Ravindran
Sanuj K. Ravindran, M.D.

Ex. A - 9

THIRD AMENDMENT TO

LOAN AND SECURITY AGREEMENT

THIS **THIRD AMENDMENT** to Loan and Security Agreement (this "**Amendment**") is entered into as of December 22, 2017, by and between **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 of the Loan Agreement (as defined below) or otherwise party thereto from time to time (each a "**Lender**" and collectively, the "**Lenders**") 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 **ATYR PHARMA, INC.**, a Delaware corporation with offices located at 3545 John Hopkins Court, Suite 250, San Diego, CA 92121 ("**Borrower**").

Recitals

A. Collateral Agent, Lenders and Borrower have entered into that certain Loan and Security Agreement dated as of November 18, 2016 (as amended from time to time, including but not limited to that certain First Amendment to Loan and Security Agreement dated as of June 30, 2017 and that certain Second Amendment to Loan and Security Agreement dated as of October 10, 2017, the "**Loan Agreement**").

B. Lenders have extended credit to Borrower for the purposes permitted in the Loan Agreement.

C. Borrower has requested that Collateral Agent and Lenders (i) modify the Third Draw Period Milestones Definition and (ii) make certain other revisions to the Loan Agreement as more fully set forth herein.

D. Collateral Agent and Lenders have agreed to modify such consent and to amend certain provisions of the Loan Agreement, but only to the extent, in accordance with the terms, subject to the conditions and in reliance upon the representations and warranties set forth below.

Agreement

Now, Therefore, in consideration of the foregoing recitals and other good and valuable consideration, the receipt and adequacy of which is hereby acknowledged, and intending to be legally bound, the parties hereto agree as follows:

1. Definitions. Capitalized terms used but not defined in this Amendment shall have the meanings given to them in the Loan Agreement.

2. Amendment to Loan Agreement.

2.1 Section 6.10 (Phase 1 Trial Initiation). Section 6.10 is hereby amended and restated in its entirety as follows:

"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, Australia or the European Union."

2.2 Section 13.1 (Definitions). The following term and its definition hereby are amended and restated in their entirety, to Section 13.1 of the Loan Agreement as follows:

"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, the European Union, or Australia, 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.

3. Limitation of Amendment.

3.1 The amendment set forth in **Section 2** above is effective for the purposes set forth herein and shall be limited precisely as written and shall not be deemed to (a) be a consent to any amendment, waiver or modification of any other term or condition of any Loan Document, or (b) otherwise prejudice any right or remedy which Collateral Agent or any Lender may now have or may have in the future under or in connection with any Loan Document.

3.2 This Amendment shall be construed in connection with and as part of the Loan Documents and all terms, conditions, representations, warranties, covenants and agreements set forth in the Loan Documents, except as herein amended, are hereby ratified and confirmed and shall remain in full force and effect.

4. Representations and Warranties. To induce Collateral Agent and Lenders to enter into this Amendment, Borrower hereby represents and warrants to Collateral Agent and Lenders as follows:

4.1 Immediately after giving effect to this Amendment (a) the representations and warranties contained in the Loan Documents are true and correct in all material respects as of the date hereof (except to the extent such representations and warranties relate to an earlier date, in which case they are true and correct in all material respects as of such date), and (b) no Event of Default has occurred and is continuing;

4.2 Borrower has the power and authority to execute and deliver this Amendment and to perform its obligations under the Loan Agreement, as amended by this Amendment;

4.3 The organizational documents of Borrower delivered to Collateral Agent and Lenders on the date hereof are true, accurate and complete and have not been amended, supplemented or restated and are and continue to be in full force and effect;

4.4 The execution and delivery by Borrower of this Amendment and the performance by Borrower of its obligations under the Loan Agreement, as amended by this Amendment, have been duly authorized;

4.5 The execution and delivery by Borrower of this Amendment and the performance by Borrower of its obligations under the Loan Agreement, as amended by this Amendment, do not and will not contravene (a) any material Requirement of Law binding on or affecting Borrower, (b) any material agreement with a Person binding on Borrower, (c) any order, judgment or decree of any court or other governmental or public body or authority, or subdivision thereof, binding on Borrower, or (d) the organizational documents of Borrower;

4.6 The execution and delivery by Borrower of this Amendment and the performance by Borrower of its obligations under the Loan Agreement, as amended by this Amendment, do not require any order, consent, approval, license, authorization or validation of, or filing, recording or registration with, or exemption by any governmental or public body or authority, or subdivision thereof, binding on Borrower (except as have been made or obtained prior to the date hereof or are being obtained pursuant to Section 6.1(b) of the Loan Agreement or which the failure to obtain or make could not reasonably be expected to result in a Material Adverse Effect); and

4.7 This Amendment has been duly executed and delivered by Borrower and is the binding obligation of Borrower, enforceable against Borrower in accordance with its terms, except as such enforceability may

be limited by bankruptcy, insolvency, reorganization, liquidation, moratorium or other similar laws of general application and equitable principles relating to or affecting creditors' rights.

5. Counterparts. This Amendment may be executed in any number of counterparts and all of such counterparts taken together shall be deemed to constitute one and the same instrument.

6. Effectiveness. This Amendment shall be deemed effective upon the due execution and delivery to Collateral Agent and Lenders of (i) this Amendment by each party hereto and (ii) Borrower's payment of all Lenders' Expenses incurred through the date of this Amendment.

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In Witness Whereof, the parties hereto have caused this Amendment to be duly executed and delivered as of the date first written above.

COLLATERAL AGENT AND LENDER:

SILICON VALLEY BANK

By: /s/ Anthony Flores

Name: Anthony Flores

Title: Director

LENDER:

SOLAR CAPITAL LTD.

By: /s/ Anthony J. Storino

Name: Anthony Storino

Title: Authorized Signatory

BORROWER:

ATYR PHARMA, INC.

By: /s/ John Blake

Name: John Blake

Title: Sr. Vice President, Finance

[Signature Page to Third Amendment to Loan and Security Agreement]

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CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in the following Registration Statements:

1. Registration Statements (Form S-3 Nos. 333-211998 and 333-220463) 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,
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, and
4. Registration Statement (Form S-8 No. 333-216880) pertaining to the ATYR PHARMA, INC. 2015 STOCK OPTION AND INCENTIVE PLAN, the ATYR PHARMA, INC. 2015 EMPLOYEE STOCK PURCHASE PLAN, and the NON-QUALIFIED STOCK OPTION INDUCEMENT AWARD;

of our report dated March 20, 2018, 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, 2017.

/s/ Ernst & Young LLP

San Diego, California
March 20, 2018

**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, Sanjay S. Shukla, 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 provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
 - c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
 - d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
 - a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
 - b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 20, 2018

/s/ Sanjay S. Shukla

Sanjay S. Shukla, M.D., M.S.
President, Chief Executive Officer and Director
(Principal Executive Officer)

**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 provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
 - c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
 - d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
 - a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
 - b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 20, 2018

/s/ John T. Blake

John T. Blake
(Principal Financial and Accounting Officer)

**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, 2017, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Sanjay S. Shukla, President, Chief Executive Officer and Director 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 20, 2018

/s/ Sanjay S. Shukla

Sanjay S. Shukla, M.D., M.S.

President, Chief Executive Officer and Director

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.

**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, 2017, 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 20, 2018

/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.

