

**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
WASHINGTON, D.C. 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, 2019

or

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

For the transition period from \_\_\_\_\_ to \_\_\_\_\_

Commission file number: 001-37378

**ATYR PHARMA, INC.**

(Exact name of registrant as specified in its charter)

Delaware  
(State or other jurisdiction of  
incorporation or organization)

3545 John Hopkins Court, Suite #250, San Diego, CA  
(Address of principal executive offices)

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

92121  
(Zip Code)

Registrant's telephone number, including area code (858) 731-8389

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

Title of each class	Trading Symbol	Name of each exchange on which registered
Common Stock, par value \$0.001 per share	LIFE	The Nasdaq Capital 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 every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files).  
 Yes  No

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

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

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

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

The aggregate market value of the registrant's common stock held by non-affiliates of the registrant was approximately \$10,206,392 based on the closing price of the registrant's common stock on the Nasdaq Capital Market of \$5.13 per share on June 28, 2019, the last business day of the registrant's most recently completed second quarter. Shares of common stock held by each executive officer and director 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 19, 2020 was 9,352,498.

**DOCUMENTS INCORPORATED BY REFERENCE**

Portions of the registrant's proxy statement to be filed with the Securities and Exchange Commission (SEC), pursuant to Regulation 14A in connection with the registrant's 2020 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, 2019.

ANNUAL REPORT ON FORM 10-K  
For the Fiscal Year Ended December 31, 2019

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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 our 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. 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 Annual Report 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

In addition to historical information, this Annual Report and the information incorporated herein by reference contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (the Securities Act) and Section 21E of the Securities Exchange Act of 1934, as amended (the Exchange Act) including statements regarding our business, our financial position, the research and development of biopharmaceutical products, the timing of clinical trial activities and other statements describing our goals, expectations, intentions or beliefs. These statements include but are not limited to statements under the captions “Business” and “Management’s Discussion and Analysis of Financial Condition and Results of Operations”, as well as other sections in this Annual Report. Such statements reflect our current views and assumptions and are subject to risks and uncertainties, particularly those inherent in the process of developing and commercializing biopharmaceutical products. Actual results could differ materially from those discussed in this Annual Report. Factors that could cause or contribute to such differences include, but are not limited to, those identified in Item 1A entitled “Risk Factors” beginning on page 23 of this Annual Report, as well as those discussed in our other filings with the Securities and Exchange Commission (SEC) including our Quarterly Reports on Form 10-Q. As a result, you are cautioned not to unduly rely on these forward-looking statements. We disclaim any duty to update any forward-looking statement to reflect events or circumstances that occur after the date on which such statement is made.

**Item 1. Business.**

We are a biotherapeutics company engaged in the discovery and development of innovative medicines based on novel immunological pathways. We have concentrated our research and development efforts on a newly discovered area of biology, the extracellular functionality and signaling pathways of tRNA synthetases. 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 a potential pipeline of protein compositions derived from 20 tRNA synthetase genes and their extracellular targets, such as neuropilin-2 (NRP2).

Our primary focus is on ATYR1923, a clinical stage product candidate which binds to the NRP2 receptor and is designed to down regulate immune engagement in interstitial lung diseases (ILDs). ATYR1923, a fusion protein comprised of the immuno-modulatory domain of histidyl tRNA synthetase (HARS) fused to the fragment crystallizable (FC) region of a human antibody, is a selective modulator of NRP2 that downregulates the innate and adaptive immune response in inflammatory disease states. We are developing ATYR1923 as a potential therapeutic for patients with ILDs, a group of immune-mediated disorders that cause progressive fibrosis of the lung tissue. We selected pulmonary sarcoidosis as our first ILD indication and are currently enrolling a proof-of-concept Phase 1b/2a clinical trial in patients. The study has been designed to evaluate the safety, tolerability and immunogenicity of multiple doses of ATYR1923 and to evaluate established clinical endpoints and certain biomarkers to assess preliminary activity of ATYR1923. A blinded interim analysis of safety and tolerability, the primary endpoint of our ongoing Phase 1b/2a clinical trial, showed study drug (ATYR1923 or placebo) was observed to be generally well tolerated with no drug-related serious adverse events (SAEs), consistent with the earlier Phase 1 study results in healthy volunteers. The final results of our current Phase 1b/2a clinical trial will guide future development of ATYR1923 in pulmonary sarcoidosis and provide insight for the potential of ATYR1923 in other ILDs, such as chronic hypersensitivity pneumonitis (CHP) and connective tissue disease ILD (CTD-ILD).

In January 2020, we entered into a license with Kyorin Pharmaceutical Co., Ltd. (Kyorin) for the development and commercialization of ATYR1923 for ILDs in Japan. Under the collaboration and license agreement with Kyorin (the Kyorin Agreement), Kyorin received an exclusive right to develop and commercialize ATYR1923 in Japan for all forms of ILDs. We received an \$8.0 million upfront payment and we are eligible to receive an additional \$167.0 million in the aggregate upon achievement of certain development, regulatory and sales milestones, as well as tiered royalties ranging from the mid-single digits to mid-teens on net sales in Japan. Under the terms of the Kyorin Agreement, Kyorin will fund all research, development, regulatory, marketing and commercialization activities in Japan, as well as support our global development efforts for ATYR1923.

In conjunction with our clinical development of ATYR1923, we have in parallel been expanding our knowledge of NRP2 antibodies and tRNA synthetases.

NRP2 is a receptor that plays a key role in lymphatic development and in regulating inflammatory responses. In many forms of cancer, high NRP2 expression is associated with worse outcomes. NRP2 can interact with multiple ligands and coreceptors to influence their functional roles. We are actively investigating NRP2 receptor biology, both internally and in collaboration with key academic thought leaders, to identify new product candidates for a variety of disease settings, including cancer, inflammation, and lymphangiogenesis. We have generated a panel of certain NRP2 antibodies that we believe have potential therapeutic value in oncology and are currently evaluating such antibodies in experimental models. We are also working closely with other collaborators and academia to further research in these areas. For example, in January 2019, we expanded a successful pilot study and entered into a research collaboration with the University of Nebraska Medical Center (UNMC) and Dr. Kaustubh Datta, who has published extensively in the field of NRP2 biology. In October 2019, we entered into a research collaboration with Dr. Diane Bielenberg at Boston Children's Hospital, an expert in NRP2 biology, to examine the therapeutic efficacy of anti-NRP2 antibodies in potential new roles and indications. Dr. Bielenberg's research will initially explore conditions characterized by inappropriate smooth muscle contractility, such as urinary incontinence and gastrointestinal tract motility disorders, where current treatments often have limited efficacy and serious side effects.

Our continued research of tRNA synthetases is being conducted through both industry and academic collaborations. In March 2019, we entered into a research collaboration and option agreement with CSL Behring (CSL) for the development of product candidates derived from up to four tRNA synthetases from our preclinical pipeline. Under the terms of the collaboration, CSL is obligated to fund all research and development activities and will pay a total of \$4.25 million per synthetase program (\$17.0 million if all four synthetase programs advance) in option fees based on achievement of research milestones and CSL's determination to continue development.

## Therapeutic Candidate Pipeline



## Strategy

Key elements of our strategy include the following:

**Develop ATYR1923 to address unmet medical needs within interstitial lung diseases.** We believe that by establishing proof-of-concept in pulmonary sarcoidosis, we can gain insight to the potential of ATYR1923 in other ILDs, such as CHP and CTD-ILD. Our resources are devoted to completing our ATYR1923 Phase 1b/2a clinical trial and, if that trial is successful, we believe we can expedite development of ATYR1923 for pulmonary sarcoidosis towards regulatory approval. In addition, success in our ATYR1923 Phase 1b/2a trial and our Kyorin Agreement, could give us the opportunity to potentially launch additional Phase 2 clinical trials for both CHP and CTD-ILD.

**Expand our knowledge on the therapeutic potential of NRP2 antibodies by utilizing our leadership position in this emerging area of biology.** NRP2 is a receptor that plays a key role in lymphatic development and in regulating inflammatory responses. In many forms of cancer, high NRP2 expression is associated with worse outcomes. These associations may represent new therapeutic drug opportunities. We are committed to translating this groundbreaking area of newly discovered biology to therapeutic applications, both with our internal research and through academic collaborations, such as our research collaboration with Dr. Beilenberg and Boston Children's Hospital.

**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 based on tRNA synthetases with the goal of developing programs with multiple therapeutic modalities. We intend to work with both industry and academic collaborators to further product development in this area. Our collaboration with CSL will explore the potential to develop programs from up to four additional tRNA synthetases from our preclinical pipeline.

## ATYR1923

### Overview of ATYR1923

We are initially developing ATYR1923 as a potential therapeutic for patients with ILD, a group of immune-mediated disorders that cause progressive fibrosis of the lung tissue. ATYR1923 is a selective modulator of NRP2 that downregulates the innate and adaptive immune response in inflammatory disease states. We announced data from a first-in-human Phase 1 clinical trial of ATYR1923 in June 2018. This randomized, double-blind, placebo-controlled study investigated the safety, tolerability, immunogenicity, and pharmacokinetics (PK) of intravenous ATYR1923 in 36 healthy volunteers. The results indicate that the drug was generally well-tolerated at all dose levels tested, with no significant adverse events and the observed PK profile supports the potential for a once-monthly dosing regimen.

In parallel with the Phase 1 clinical trial, we demonstrated the therapeutic potential of ATYR1923 in a number of preclinical models of lung injury and inflammation in rodents. For example, we presented the positive results in a mouse bleomycin lung injury model and a rat bleomycin lung injury model at the 2017 and 2018 American Thoracic Society (ATS) Annual Meetings, respectively. In addition, we presented positive findings in a sclerodermatous chronic graft versus host disease model at the Scleroderma Foundation's 2018 National Patient Conference. At the 2019 ATS Annual Meeting, we presented data that indicated ATYR1923 has a stage-dependent anti-inflammatory and anti-fibrotic effect in various experimental models of ILD.

A comprehensive review of this data in consultation with key opinion leaders led to our selection of pulmonary sarcoidosis as the first ILD indication for our ATYR1923 Phase 1b/2a clinical trial program.

We are currently enrolling a proof-of-concept Phase 1b/2a clinical trial of ATYR1923 in 36 patients with pulmonary sarcoidosis. This Phase 1b/2a study is a multiple-ascending dose, placebo-controlled, first-in-patient study of ATYR1923 that has been designed to evaluate the safety, tolerability, immunogenicity and PK profile of multiple doses of ATYR1923. In December 2019, we conducted a pre-planned, blinded interim analysis of safety and tolerability, the primary endpoint of our ongoing Phase 1b/2a clinical trial, which showed study drug (ATYR1923 or placebo) was observed to be generally well tolerated with no drug-related SAEs, consistent with the earlier Phase 1 study results in healthy volunteers. Secondary endpoints include the evaluation of steroid sparing effect and other established clinical endpoints along with potential biomarkers to assess preliminary activity of ATYR1923.

#### *Background and Mechanism of Action*

ATYR1923 is a selective modulator of NRP2 that downregulates the innate and adaptive immune response in inflammatory disease states.

The ATYR1923 program was initiated to leverage our knowledge of the extracellular proteins derived from the HARS family (Resokine pathway) to develop a therapeutic which would possess the N-terminal immuno-modulatory activities of HARS.

The Resokine family of proteins is derived from the HARS gene via proteolysis or alternative splicing. We believe these splice variants are important modulators of innate and adaptive immune activation. Proteins derived from the HARS gene, including both full-length and splice variants, are present in circulation. We refer to the extracellular HARS proteins as Resokine, to differentiate them from the intracellular enzyme involved in protein synthesis. Our scientists were the first to discover the novel immunomodulatory role of the Resokine pathway.

The gene for HARS gives rise to a number of splice variants, and though most of these have lost their catalytic activity, many retain the N-terminal domain (iMod domain). This N-terminal domain was appended to HARS during evolutionary development of multicellular organisms and is not essential for protein synthetic activity, is not generally found in prokaryotic organisms, and is retained with high homology across mammalian species. Alternative splicing of HARS may be differentially regulated during cellular growth and differentiation, unlike the constitutive high level expression of the full length protein, suggesting that these splice variants may play a differential role in growth and cellular development.

Recently, significant progress has been made in elucidating the role of extracellular HARS derived proteins, including the identification of a putative cellular receptor of the iMod domain through screening via a cell microarray system in which over 4,000 cell surface proteins are represented. This screening approach identified two NRP2 isoforms (Neuropilin 2A and 2B) as the only convincing and specific binding partners of the iMod domain. Interactions of HARS with NRP2 appear to be specifically mediated by the iMod domain of HARS, and binding of the iMod domain of HARS is specific to NRP2 with no observable binding to NRP1, which is the most closely related cell surface receptor. A domain that is structurally similar to the iMod domain (termed the WHEP domain) is found in other amino-acyl tRNA synthetases, yet these domains do not exhibit binding to NRP2, indicating this is a highly specific interaction. The discovery of the Resokine/NRP2 axis represents a previously unknown mechanism of biological regulation, which may act as a homeostatic regulator of several cellular processes mediated through the neuropilin receptor. The deregulation of these processes may lead to a spectrum of diseases, which could be selectively targeted by modulating the Resokine/NRP2 axis to address the underlying disease etiology.

NRP2 is a pleiotropic co-receptor participating in a broad array of biological pathways including, immunomodulation, lymphangiogenesis, neuronal development and remodeling, cellular growth, migration and differentiation, and cancer development. These biological processes are mediated through a complex interplay of several signaling systems including the semaphorins/plexin receptor family, the VEGF-C/VEGFR3 receptor family, as well as CCL21 driven trafficking and integrin signaling pathways. Growing evidence indicates that NRP2 influences myeloid cell biology such as activation and recruitment to inflammatory sites. For instance, NRP2 expression on alveolar macrophages regulates airway inflammatory responses to inhaled LPS.

ATYR1923 development builds upon our understanding of the biology of the extracellular activity of HARS. This novel molecular entity acts as a selective modulator of NRP2 downregulating the innate and adaptive immune response in inflammatory

disease states. ATYR1923 is a fusion protein comprised of the immuno-modulatory domain of HARS fused to the FC region of a human antibody.

### *Preclinical Development*

Our preclinical development estate of translational animal models were selected to help inform and de-risk clinical development of ATYR1923. We have evaluated the biological activity and safety of ATYR1923 across a diverse set of experimental lung disease models, as well as in normal animals, looking for signals of activity and potential biomarkers, while confirming tolerability and a favorable safety profile.

#### Bleomycin-Induced Lung Injury in Mice

ATYR1923 significantly reduced lung fibrosis and inflammation in two bleomycin-induced lung injury models in mice. The bleomycin-induced lung injury model has been used as a translational model previously in the development of therapeutics for ILD, including the drugs pirfenidone, or Esbriet®, and nintedanib, or Ofev®, which were both approved by the U.S. Food and Drug Administration (FDA) in October 2014 for the treatment of idiopathic pulmonary fibrosis (IPF). ATYR1923 administered therapeutically in this model drives activity comparable to or greater than pirfenidone, anti-TGF antibodies, and dexamethasone. These preclinical experiments were presented in a poster at the ATS International Congress in Washington D.C. in May 2017.

#### Bleomycin-Induced Lung Injury in Rats

ATYR1923 significantly reduced lung fibrosis and inflammation and improved lung function in a bleomycin-induced lung injury model in rats. The rat bleomycin-induced model allows for analysis of functional endpoints, such as breathing rate, which is not possible in mice. Data demonstrated that ATYR1923, administered starting on Day 1 or Day 9, returned lung function to normal as measured by respiratory minute volume, a measure of breathing rate that is exacerbated in inflammatory conditions. In contrast, nintedanib was ineffective at reducing both fibrosis and interstitial/alveolar inflammation in these animals. These results may indicate that treatment with ATYR1923 during an inflammatory phase of the model may be beneficial for reducing inflammation-dependent fibrosis. This experiment was presented in a poster at the ATS International Congress in San Diego, CA in May 2018.

#### Sclerodermatous Chronic Graft vs. Host Disease Model (SSc-cGVHD) in Mice

ATYR1923 significantly reduced measures of lung and skin fibrosis in a sclerodermatous chronic graft vs host disease model in mice, with early administration. We employed a minor histocompatibility antigen mismatched model which has been reported to mimic many of the pathological symptoms of human disease. Weekly intravenous treatment with ATYR1923, at 0.4 mg/kg, was compared with daily oral nintedanib, at 60 mg/kg, with administration beginning at Day 7 for early intervention or at Day 21 for late intervention.

ATYR1923, beginning on Day 7, exhibited robust and consistent therapeutic activity in both skin and lung, demonstrated by significantly decreased dermal thickness in the skin and histological fibrosis or Ashcroft score in the lungs in comparison to the untreated controls. The number of myofibroblasts and amount of hydroxyproline (i.e., collagen) content was also significantly reduced in both organs. Observed effects with weekly dosing of ATYR1923 were similar to those observed with daily dosing of nintedanib. Late intervention with ATYR1923 at 0.4 mg/kg was not significantly effective with this dosing paradigm, consistent with our hypothesis that ATYR1923 may be most active during the active inflammatory phase of disease. In this model the damage to both lung and skin is indirect from a systemic GvHD reaction, and yet we observed consistent therapeutic activity with ATYR1923, supporting our therapeutic hypothesis that ATYR1923 can downregulate the immune response and inflammation following tissue injury and prevent progression to fibrosis, which presents an attractive drug profile for treating ILD.

Data from this model was presented at the Scleroderma Foundation National Patient Education Conference in Philadelphia, PA in July 2018. The results from this systemic disease model are consistent with direct lung injury models presented previously at ATS in 2017 and in 2018.

#### SSc-cGVHD (SSc-ILD); P. acnes (Sarcoidosis); S. rectivirgula (CHP); SKG (Ra-ILD) in Mice

ATYR1923 was evaluated in the following murine models of ILD: Sclerodermatous chronic graft-versus-host disease (scl cGvHD), Saccharopolyspora rectivirgula-induced CHP, Propionibacterium acnes-induced pulmonary fibrosis (sarcoidosis) and SKG mice rheumatoid arthritis-associated interstitial lung disease, (RA-ILD). ATYR1923 was given intravenously once a week at 0.4 - 3 mg/kg.

In the sclerodermatous cGvHD model, low-dose ATYR1923 (0.4 mg/kg) significantly decreased both skin and lung fibrosis as determined by histopathological and biochemical analyses. Likewise, ATYR1923 reduced lung protein levels of several fibrosis-related cytokines or chemokines (e.g. IFN- $\gamma$ , MCP-1/CCL2, IL-6, CXCL10) in the highly inflammatory experimental CHP and sarcoidosis models. In addition, flow cytometric analysis of cells isolated from lungs of SKG mice showed significantly lower numbers of lymphocytes in ATYR1923 treated animals.

ATYR1923 has pharmacological activity in a murine model of sclerodermatous cGvHD when dosed during the active inflammatory phase of the model. Furthermore, protein and cellular analyses indicate that ATYR1923 has potent immunomodulatory activity in other animal models of ILD and that these effects were most prominent in models that are highly inflammatory or T cell driven. These data are compatible with our hypothesis that ATYR1923 modulates inflammatory responses that may lead to subsequent downstream inhibition of fibrosis, as observed in the sclerodermatous GvHD model.

These experiments were presented in a poster at the ATS International Congress in Dallas, TX in May 2019.

Based on our translational biology program, with activity across distinct experimental animal models either driven by direct lung injury or systemic pathology, along with our understanding of the ATYR1923 and NRP2 interaction and the cell types involved in the mechanism of action of our drug, we decided to move the program forward into patient trials. A comprehensive review of this translational data in consultation with key opinion leaders led to our selection of pulmonary sarcoidosis as the first ILD indication for our ATYR1923 Phase 1b/2a clinical trial program.

#### *ILDs, Pulmonary Sarcoidosis, and the Role of Immunology*

ILDs are a group of immune-mediated disorders which cause progressive fibrosis of lung tissue. There are over 100 different types of ILD, of which the four major forms are: pulmonary sarcoidosis, CTD-ILD, CHP and idiopathic pulmonary fibrosis. Among the various forms of ILD, we have focused on several that result in severe and progressive lung disease and share immune-pathophysiology features that have the potential to be impacted by ATYR1923 as demonstrated in our preclinical models. These lung conditions are recognized as having a measurable immune component involving both innate and adaptive immune mechanisms that contribute to pathogenesis at several cellular and non-cellular levels, and can result in progressive disease leading to fibrosis and death. The first ILD that we are focusing on clinically is pulmonary sarcoidosis.

The immunopathogenesis of sarcoidosis is not yet well understood. A leading hypothesis is that granuloma formation involves the interplay between antigen, human leukocyte antigen (HLA) class II molecules, and T-cell receptors: a presumptive sarcoid antigen is engulfed by circulating antigen-presenting cells (APCs; macrophages, dendritic cells) and the subsequent interplay between APCs and CD4+ T-cells initiates granuloma formation. T lymphocyte activation subsequently plays a crucial role in sarcoidosis pathogenesis.

Sarcoidosis affects people of all ages, but typically presents before the age of 50 years, with the incidence peaking at 20 to 39 years. The disorder usually begins in the lungs, skin or lymph nodes, but can affect almost any organ. Sarcoidosis in the lungs is called pulmonary sarcoidosis and 90% or more of patients with sarcoidosis have lung involvement. Pulmonary sarcoidosis is a major form of ILD. Estimates of prevalence vary; however, we believe that approximately 200,000 Americans live with pulmonary sarcoidosis. The prognosis for patients with pulmonary sarcoidosis ranges from benign and self-limiting to chronic, debilitating fibrotic disease and mortality.

For patients with pulmonary sarcoidosis, the primary goal of treatment is typically to improve the patient's quality of life, while secondarily managing the inflammation associated with the granulomas that could lead to the development of more permanent fibrosis and impairment of pulmonary function. ATYR1923 may provide a therapeutic benefit in pulmonary sarcoidosis by providing an immunomodulatory function to help resolve inflammation. Moreover, the mechanism of action of ATYR1923 in T-cells and macrophages potentially overlaps with the cellular pathology observed in pulmonary sarcoidosis. In preclinical studies, ATYR1923 has been observed to inhibit cytokines involved in regulation of inflammatory and immune responses and attenuate T-cell activation, while also modulating macrophage endosome maturation. Related to our mechanistic studies, we have also discovered that NRP2 is up-regulated during activation of myeloid cells including macrophages, dendritic cells and neutrophils, and that ATYR1923 can bind to NRP2 on these cell types. Furthermore, ATYR1923 has been observed to significantly reduce inflammation-dependent pulmonary fibrosis and improve respiratory function parameters in bleomycin-induced animal models of ILD, particularly when administered during the inflammatory phase of the disease. Accordingly, based on these data, we believe that by inhibiting the inflammatory portion of the fibrotic cascade, ATYR1923 could provide a safer, potentially more effective alternative with less toxic effects as compared to oral corticosteroids and other immunosuppressive therapies for patients with symptomatic pulmonary sarcoidosis and prevent progression to fibrosis.

#### *Clinical Development*

##### ATYR1923 Phase 1 Clinical Trial

In June 2018, we announced results of our first-in-human Phase 1 clinical trial of ATYR1923 conducted in Australia. This randomized, double-blind, placebo-controlled study evaluated the safety, tolerability, immunogenicity, and PK of intravenous (IV) ATYR1923 in healthy volunteers. The Phase 1 study enrolled 36 healthy volunteers who were randomized to one of six sequential cohorts and received a single infusion of intravenous ATYR1923 or placebo. Ascending ATYR1923 doses by cohort ranged from 0.03 mg/kg to 5.0 mg/kg. The results indicate that the drug was generally well-tolerated at all dose levels tested, with no significant adverse events or induction of anti-drug antibodies observed following ATYR1923 dosing or throughout the one-month follow-up period. The



PK of ATYR1923 following single-dose administration were linear across the evaluated dose range. Higher ATYR1923 doses yielded sustained serum concentrations through the end of the one-month follow-up period that were above the predicted therapeutic threshold, supporting the potential for a once-monthly dosing regimen.

In parallel, as described above we expanded 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 translational research data, as well as the Phase 1 clinical trial results and discussions with key opinion leaders, helped to guide our development plans for ATYR1923. In September 2018, we announced pulmonary sarcoidosis as the indication for our next study.

#### ATYR1923 Phase 1b/2a Clinical Trial

We initiated a proof-of-concept Phase 1b/2a clinical trial for ATYR1923 in December 2018 following FDA acceptance of our investigational new drug application (IND) filed in October 2018. The Phase 1b/2a clinical trial is a randomized, double-blind, placebo-controlled multiple-ascending dose, first-in-patient study with IV ATYR1923 in 36 patients. The study is being conducted in patients with pulmonary sarcoidosis undergoing an oral corticosteroids (OCS) tapering regimen, in three cohorts of 12 patients each, at dose levels of 1.0 mg/kg, 3.0 mg/kg and 5.0 mg/kg.

The primary objective of the study is to evaluate safety and tolerability of multiple ascending doses of ATYR1923. Secondary objectives include assessment of the potential steroid-sparing effects of ATYR1923. In addition, ATYR1923 PK and immunogenicity following multiple dose administration will be evaluated. Additional endpoints of interest include the exploratory assessment of the efficacy of ATYR1923 for the treatment of pulmonary sarcoidosis by evaluating changes over time in: fluorodeoxyglucose-positron emission tomography (FDG-PET)/CT lung imaging; lung function assessed by percent predicted FVC (FVC%) and diffusing capacity of the lungs for carbon monoxide (DLCO); serum biomarkers of interest; health-related quality of life assessments and questionnaires; and measurement of skin lesions (for patients with cutaneous involvement at baseline).

This study consists of three staggered dose cohorts. Each cohort will consist of three periods: a screening period, a 20-week placebo-controlled treatment period, and a four-week follow-up period ending with final study assessments at Week 24. Within each cohort, 12 patients will be randomized 2:1 to ATYR1923 (N=8) or placebo (N=4). Study drug will be administered via IV infusion every four weeks for a total of six doses (20 weeks of treatment). The ATYR1923 doses levels to be evaluated are 1.0 mg/kg, 3.0 mg/kg and 5.0 mg/kg. Approximately 36 patients will be enrolled. Starting on Day 15 patients will begin a taper (reduction) in OCS according to specific guidelines from their starting dose of 10-25 mg/day of prednisone (or equivalent) to a target dose of 5.0 mg/day, to be completed on or before Day 50. The OCS dose will be tapered through Week 24 and patients will be followed for the remainder of the study to determine their ability to maintain on this 5.0 mg dose. Optionally, further reductions in the OCS dose to below 5.0 mg/day may be attempted after the Week 16 visit, if determined by the investigator to be feasible. Patients who require an increase in OCS dose at any time in the study should continue to receive blinded study drug and be followed through to the end of the study.

Cohorts 1 through 3 will be enrolled sequentially in a staggered manner. After a minimum of six patients of a given cohort have received at least three intravenous infusions of study drug (ATYR1923 or placebo), cumulative unblinded safety data will be reviewed by a data safety monitoring board (DSMB). Enrollment in the next scheduled (higher dose) cohort may commence after this review is completed, dose escalation is approved by the DSMB, and the remaining six patients have been enrolled in the current cohort. Dose escalation will continue in this manner until the highest planned dose level of ATYR1923 is reached, or the criteria for pausing enrollment have been met.

In December 2019, we announced the results of a pre-planned, blinded interim analysis of safety and tolerability, the primary endpoint of our Phase 1b/2a clinical trial. Study drug (ATYR1923 or placebo) was observed to be generally well tolerated with no drug-related SAEs, consistent with the earlier Phase 1 study results in healthy volunteers. Adverse events (AEs) were mostly mild or moderate in severity and assessed by the study investigators as unrelated to study drug. Interim safety data results were from 15 pulmonary sarcoidosis patients who had received a minimum of one dose of blinded study drug (ATYR1923 or placebo). The average age of patients evaluated was approximately 51 years. The patient population consisted of 53% males and 47% females, of which 73% were Caucasian and 27% were African American. No induction of anti-drug antibodies was observed with repeat dosing of study drug. There were no notable trends for clinical laboratory values or vital signs. Having accomplished this first important interim step in our study, we are now focused on demonstrating activity of ATYR1923 and advancing our trial to provide evidence of the potential of ATYR1923 as a treatment option to improve the lives of patients with pulmonary sarcoidosis.

We are collaborating with the Foundation for Sarcoidosis Research (FSR), a leading nonprofit organization dedicated to finding a cure for sarcoidosis and improving care for sarcoidosis patients. Under the terms of the collaboration, FSR is assisting with clinical trial site initiation and patient enrollment for our ATYR1923 Phase 1b/2a clinical trial. We have 17 sites in the United States participating in the study. FSR's Clinical Studies Network (FSR-CSN), which is led by a steering committee consisting of principal investigators from leading clinical centers, has voted to support this proof-of-concept study.

While the trial continues to progress, as a result of the recent COVID-19 outbreak in the United States, many clinical trial sites in our ongoing Phase 1b/2a clinical trial have temporarily suspended dosing of previously-enrolled patients and/or enrollment of new patients. As a result, we anticipate that the availability of top-line results from the clinical trial will be delayed. We are in close contact with our clinical trial sites as we assess and attempt to mitigate the impact of COVID-19 on our clinical trial, including the scope of any delays.

### Kyorin Agreement

In January 2020, we entered the Kyorin Agreement for the development and commercialization of ATYR1923 for ILDs in Japan.

Pursuant to the terms of the Kyorin Agreement, Kyorin received an exclusive right to develop and commercialize ATYR1923 in Japan for ILDs and will be responsible for funding associated costs for research, development, regulatory, marketing and commercialization activities in Japan. We are responsible for supplying all drug product for Japan, as well as supporting development activities for ATYR1923. We received an \$8.0 million upfront payment and we are eligible to receive up to an additional \$167.0 million in the aggregate upon achievement of certain development, regulatory and sales milestones, as well as tiered royalties ranging from the mid-single digits to mid-teens on net sales in Japan. The royalty obligations continue on a product-by-product basis until the earlier of the last to expire of the applicable licensed patents, the entry of a generic product in Japan, the expiration of any regulatory exclusivity period and ten years after the first commercial sale of the product in Japan.

Unless earlier terminated, the term of the Kyorin Agreement continues until the expiration of the royalty obligations. Following the first anniversary of the effective date of the Kyorin Agreement, Kyorin has the right to terminate the agreement for any reason upon 90 days advance written notice to the Company. Either party may terminate the Kyorin Agreement in the event that the other party breaches the agreement and fails to cure the breach, becomes insolvent or challenges certain of the intellectual property rights licensed under the agreement.

### **Our Discovery Engines**

#### *NRP2 Receptor Biology*

We plan to leverage our discovery engine to identify NRP2 receptor biology 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, collaborators and academia.

NRP2 is a receptor that plays a key role in lymphatic development and in regulating inflammatory responses. In many forms of cancer, high NRP2 expression is associated with worse outcomes. NRP2 can interact with multiple ligands and coreceptors to influence their functional roles. We are actively investigating NRP2 receptor biology, both internally and in collaboration with key academic thought leaders, to identify new product candidates for a variety of disease settings, including cancer, inflammation, and lymphangiogenesis. We have generated a panel of certain NRP2 antibodies that we believe have potential therapeutic value in oncology and are currently evaluating such antibodies in experimental models.

NRP2 is a pleiotropic cell surface receptor that was originally identified based on its role in axon guidance during neuronal development, and subsequently shown to be important in the development of the lymphatic system. Importantly, NRP2 knock-out mice have been shown to have impaired lymphatic development. NRP2 can bind to multiple ligands and co-receptors to influence these multiple functional roles, including interaction with type 3 semaphorins and plexins as well as forms of vascular endothelial growth factor, especially VEGF-C which is involved in lymphogenesis, and also CCL21 (Chemokine Ligand 21). Recent evidence suggests that there are high levels of NRP2 expression found on multiple immune cell types, which may play important roles in migration of immune cells, antigen presentation, phagocytosis and cell-to-cell interactions. The role of NRP2 in the immune system has been described in several recent publications, including from the University of Technology, in Dresden, Germany (Schellenberg et al. *Mol. Immunol.* 90:239-244, 2017) and from UNMC (Roy et al, *Front. Immunol.* 8:1228, 2017). Consistent with this idea, NRP2 is expressed in various cells of the immune system such as B cells, T-cells, NK cells, neutrophils, dendritic cells and macrophages, including for example, alveolar macrophages, and plays an important role in the regulation of immune cell activation and migration (see, e.g., Mendes-da-Cruz et al., *PLoS ONE* 9(7) e103405, 2014) including endosome maturation, the modulation of autophagy and efferocytosis, (see, e.g., Stanton et al., *Cancer Res.* 73:160-171, 2013; Wang et al., *Cancer Lett.* 418 176-184 2018).

These publications suggest that NRP2 may be an important regulator of biological responses in a number of different settings with potential for therapeutic intervention. We are currently evaluating the role of the NRP2 in the control of immune responses and lymphatic development, especially within the setting of oncology. We are designing optimal therapeutic approaches to modulate this newly-discovered pathway in a number of diseases with high unmet medical need and furthering our understanding of the potential therapeutic implications of this discovery and its impact on our translational science.

## University of Nebraska Medical Center

In January 2019, we expanded a successful pilot study and entered into a research collaboration with UNMC. The laboratory of Dr. Datta at UNMC has published extensively in the NRP2 field working to elucidate the role of this receptor in tumor biology, specifically pertaining to myeloid cells. Through this collaboration we hope to broaden our understanding of the potential impact of blocking NRP2 with domain-specific antibodies in cancer.

## Boston Children's Hospital

In October 2019, we entered into a research collaboration with Dr. Diane Bielenberg, an expert in NRP2 biology, and Boston Children's Hospital to examine the therapeutic efficacy of anti-NRP2 antibodies in potential new roles and indications. Dr. Bielenberg's research will initially explore conditions characterized by inappropriate smooth muscle contractility, such as urinary incontinence and gastrointestinal tract motility disorders, where current treatments often have limited efficacy and serious side effects. Specifically, the ability of anti-NRP2 antibodies to prevent, inhibit or reverse smooth muscle decompensation in mouse models will be examined.

Hollow organs, such as the bladder or gastrointestinal (GI) tract, function to expel waste products via the action of smooth muscle contraction. Aberrant pressure, especially in the bladder, can initiate hypertrophy of the bladder wall and lead to inflammation and fibrosis with eventual decompensation in smooth muscle, increased pressure transmitted to the kidneys, and pathological renal damage. The ability of NRP2 to promote smooth muscle relaxation, along with its robust expression in hollow organs, implies that this axis could be exploited for therapeutic benefit in conditions characterized by inappropriate smooth muscle contractility.

Our team is also collaborating with other established groups working on these pathways and we are excited to learn more about NRP2 and how it may play a role in certain diseases and how it interacts with other known receptors. We will continue to research the ways in which NRP2 utilizes common mechanisms, including VEGF-C, semaphorin 3F, and CCL21 to regulate diverse pathways. We believe by increasing our understanding of the functions of NRP2 using *in vivo* experiments and building on emerging literature in this new area of biology will allow us to select and develop additional product candidates for unmet medical diseases.

## *tRNA Synthetase Biology*

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

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, our Board Member and founder, Paul Schimmel, Ph.D., and colleagues discovered that a protein derived from one of the genes for a tRNA synthetase could act as an extracellular modulator of angiogenesis. Recent research developments have further reinforced the idea that tRNA synthetases may more broadly play important roles in cellular responses beyond their well characterized role in protein synthesis. In particular, there is a growing recognition that tRNA synthetases may participate in a range of previously unrecognized roles in responding to cellular stress, and tissue homeostasis, both within the intracellular and extracellular environments.

Using ATYR1923 as a model, we have developed a process with which to advance a tRNA synthetase from a concept to a product candidate. This process leverages our early discovery data as well as current scientific literature understanding of tRNA synthetase protein structure, gene splicing and tissue-specific regulation to identify potentially active protein domains. Screening approaches are employed to identify target cells and extracellular receptors for these tRNA synthetase-derived proteins. These cellular systems can then be used in mechanism-of-action studies to elucidate the role these proteins play in cellular responses and their potential therapeutic utility. We intend to expand our knowledge of tRNA synthetase biology through both industry and academic collaborations.

## CSL

In March 2019, we entered into a research collaboration and option agreement with CSL for the development of product candidates derived from up to four tRNA synthetases from our preclinical pipeline. Under the terms of the collaboration, CSL is obligated to fund all research and development activities related to the development of the applicable product candidates for the duration of the collaboration. CSL may be obligated to pay a total of up to \$4.25 million per synthetase program (\$17.0 million if all four synthetase programs advance) in option fees based on the achievement of research milestones and CSL's determination to continue development. In addition, aTyr is obligated to grant CSL an option to negotiate licenses for worldwide rights to each IND candidate that emerges from this research collaboration. Specific license terms will be negotiated during an exclusivity period following the exercise of each program option. CSL has sole discretion to proceed to the next research phase for any synthetase program and there can be no assurance that CSL will elect to negotiate a license agreement with us for any IND candidates that result from the research collaboration.

In October 2007, we formed our Hong Kong subsidiary, Pangu BioPharma Limited (Pangu BioPharma) to support our basic and translational research in tRNA synthetase biology. We hold 98% of the outstanding shares of Pangu BioPharma, and a subsidiary of the Hong Kong University of Science and Technology (HKUST) holds the remaining outstanding shares. Pangu BioPharma originally collaborated with HKUST on the discovery and development of aminoacyl tRNA synthetase protein therapeutics. 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 2019, Pangu BioPharma amended its joint research agreement with a subsidiary of HKUST, under which Pangu BioPharma agrees to fund research to be performed in 2020 with respect to development of aminoacyl tRNA synthetase protein therapeutics.

As a result of work performed under these agreements, HKUST researchers with support from Pangu BioPharma were instrumental in discovering a splice variant of HARS that liberates the smaller, active iMod domain from the full-length tRNA synthetase and has been shown to modulate the immune system. To date, researchers at HKUST have discovered over 200 novel compositions that are covered in issued patents and have published six articles detailing their research in peer-reviewed scientific journals.

We recently announced that Pangu BioPharma, together with HKUST, was awarded a grant of approximately \$750,000 to build a high-throughput platform for the development of bi-specific antibodies. Initially this research will focus on diseases, including cancer, in which NRP2 overexpression is strongly implicated. A bi-specific antibody approach presents a further differentiated opportunity to elucidate the therapeutic potential of NRP2 and its co-receptors as drug targets. The fact that NRP2 interacts directly with various co-receptor molecules, including certain plexins, integrins and chemokine receptors like CCR7, makes it a prime target for bi-specific antibodies that can target both receptors simultaneously and modulate the activity of these signaling complexes. The two-year project is being funded by the Hong Kong Government's Innovation and Technology Commission under the Partnership Research Program. The grant will fund approximately 50% of the total estimated project cost, with aTyr contributing the remaining 50%.

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 research on a quarterly basis. Either party may terminate the agreement 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 current 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, safer 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 and NRP2 receptor biology, we are aware of other companies that could compete with our clinical stage product candidate, ATYR1923 for the treatment of pulmonary sarcoidosis and other ILDs, as described below.

### *ATYR1923*

For patients with pulmonary sarcoidosis, the primary goal of treatment is typically to improve the patient's quality of life, while secondarily managing the inflammation that could lead to the development of more permanent fibrosis and impairment of pulmonary function. Currently, the only FDA approved therapies for the treatment of sarcoidosis are prednisone, a corticosteroid, and H.P. Acthar Gel (a repository corticotropin injection marketed globally by Mallinckrodt plc), which was approved in 1952 and is not widely used by physicians due to toxicity and cost issues. The consensus standard of care are oral corticosteroids (OCS) that act mainly by suppressing inflammatory genes. OCS therapy has been shown to stabilize or improve disease symptoms, although relapse commonly occurs once OCS therapy is tapered or discontinued. Long-term OCS use is associated with significant side effects including substantial weight gain, development of insulin resistance, osteoporosis, and risk of infection. Alternatives, such as immunosuppressive and cytotoxic

agents have been used as steroid-sparing agents; however, these therapies can also have significant side effects and toxicities, including malignancies. Given the known toxicities of long-term OCS, immunosuppressives and cytotoxic therapeutic regimens, treatment of patients with sarcoidosis is limited to those who are symptomatic and whose disease is considered active. The presence of granulomas from sarcoidosis define the disease as active, and granulomatous inflammation is the major cause of fibrosis in pulmonary sarcoidosis. Studies to date have not clearly demonstrated that OCS or other immune-suppressive therapies prevent disease progression or formation of fibrosis. There exists a substantial need for safer and more effective therapies for sarcoidosis that could reduce or replace the requirement for long-term OCS therapy.

If ATYR1923 is successful for the treatment of pulmonary sarcoidosis, we believe it may have applications in other ILD indications. Immunosuppressive therapy has traditionally been used to treat most ILDs despite little evidence demonstrating safety or efficacy in these indications. We are aware of two FDA approved products with indications for the treatment of a specific form of ILD, namely idiopathic pulmonary fibrosis (IPF). Esbriet (pirfenidone), marketed globally by F. Hoffmann-La Roche Ltd., Shionogi & Co., Ltd. and ILDONG Pharmaceutical Co., Ltd., and Ofev (nintedanib), a small molecule tyrosine-kinase inhibitor marketed globally by Boehringer Ingelheim International GmbH, were both approved by FDA in October 2014 to treat IPF. Esbriet® was previously approved in Japan in 2008 and in Europe in 2011. Ofev® received an indication for another form of ILD, systemic sclerosis associated ILD (SSc-ILD) in 2019. These therapies can slow decline in lung function in controlled clinical studies but are associated with significant side effects, continued symptoms, and progressive disease in the majority of patients. There are a number of companies engaged in the clinical development of potential new therapeutics for various forms of ILD, including Novartis Pharmaceuticals Corporation, Boehringer Ingelheim International GmbH, Bristol-Myers Squibb Company, FibroGen Inc., Galapagos NV, Gilead Sciences, Inc., Mallinckrodt plc and F. Hoffmann-La Roche Ltd. among others; however, most development activity is focused on IPF, with limited activity in major forms of ILD.

## **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. For example, we recently licensed the rights to Kyorin to develop and commercialize ATYR1923 in Japan.

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 (CDMOs), and contract research organizations (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.

ATYR1923 is a fusion protein 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 current Good Manufacturing Practices (cGMP) for the successful production of ATYR1923 preclinical and clinical drug substance and drug product. We contracted with CROs to conduct labeling, storage and distribution of ATYR1923 to clinical sites.

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.

## **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 220 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, their receptors and associated signaling pathways, including, for example, antibody therapeutics to NRP2.

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, antibody 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 (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.

#### *ATYR1923*

Our ATYR1923 patent portfolio is comprised of a number of patent families related to derivatives of HARS, 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 January 2020, our ATYR1923 patent portfolio includes a patent family that is jointly owned by us and our 98% owned subsidiary, Pangu BioPharma, and includes issued patents, in the United States, Australia, China, Europe, Japan and Hong Kong, and pending patent applications in the United States, Canada, China, 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 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 issued patents in the United States, Australia, China, Japan, New Zealand and Hong Kong. Patent applications are pending in the United States and Canada. The issued patents and any 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 issued patents and pending patent applications directed to specific product forms of ATYR1923, and other HARS splice variants, including patent families directed to FC fusion proteins, and combinations for treating lung inflammation, among other indications. One family directed to specific FC fusion proteins includes issued patents in the United States, Europe, Hong Kong, and Japan, and pending applications in Australia, Canada, China Europe, Hong Kong India, and Japan. In some cases, the patent 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, the patents that derive from the patent applications are predicted to expire between 2034 and 2038, absent any patent term extensions.

Our pipeline of extracellular tRNA synthetase proteins is covered by a series of patent families, which are directed to all 20 human cytosolic tRNA synthetases. Numerous patents are issued in the United States and elsewhere, including issued U.S. patents directed to specific therapeutic protein compositions, the corresponding protein polynucleotide sequences, and certain antibody compositions to

specific splice variants. These cases are jointly owned by us and Pangu BioPharma, and include issued patents and/or pending applications in the United States, Australia, Canada, Europe, China and Japan. Patents that issue from these applications, if any, would be expected to expire in 2031, absent any patent term extension. 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 are expected to expire between 2026 and 2030, absent any patent term extension. In addition, we are actively expanding our patent portfolio directed to antibodies to NRP2, including therapeutic compositions, methods of use and diagnostic uses. Currently the anti-NRP2 patent portfolio includes two patent families directed to murine humanized antibody therapeutics. Any patents issuing from these patent applications are expected to expire between 2039 and 2040, absent any patent term extension.

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 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 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 biologics under the Federal Food, Drug, and Cosmetic Act (FDCA) and the Public Health Service Act (PHSA) and their implementing regulations. FDA approval is required before any new unapproved biologic or dosage form, including a new use of a previously approved biologic, can be marketed in the United States. 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, 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, performed in accordance with the good laboratory practice (GLP) regulations, where applicable;
- submission to the FDA of an IND which must become effective before human clinical trials may begin and must be updated annually;
- approval by an independent institutional review board (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 and conducted in accordance with good clinical practice (GCP) requirements;
- preparation of and submission to the FDA of a biologics license application (BLA) 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 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 cGMP;
- potential FDA audit of the clinical trial sites that generated the data in support of the BLA; and
- FDA review and approval of a BLA 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 or biologic 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 preclinical testing, including animal and *in vitro* studies, to assess 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 a clinical trial and may impose a partial clinical hold that would apply certain limits to the trial, for example, imposing dosage limitations or restricting the time frame of the trial.

#### *Clinical Trials*

Clinical trials involve the administration of the investigational new drug to human subjects under the supervision of qualified investigators in accordance with 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 it is 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 a relatively small number of 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. Multiple Phase 2 clinical trials may be conducted by the sponsor to obtain information prior to beginning larger and more costly Phase 3 clinical trials.



- 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, and establish the overall benefit-risk relationship of the investigational new drug product. A well-controlled, statistically robust Phase 3 trial may be designed to deliver the data that regulatory authorities will use to decide whether or not to approve, and, if approved, how to appropriately label a drug: such Phase 3 studies are referred to as “pivotal.”

In some cases, the FDA may condition approval of a BLA 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. Failure to exhibit due diligence with regard to conducting Phase 4 clinical trials that the FDA requires as a condition of approval could result in FDA withdrawing approval for the product.

A clinical trial sponsor must submit written IND safety reports to the FDA and the investigators for 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 within 15 calendar days after the sponsor determines that the information qualifies for reporting. The sponsor also must notify the FDA of any unexpected fatal or life-threatening suspected adverse reaction within seven calendar days after the sponsor’s initial receipt of the information. 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.

#### *BLA Submission*

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, detailed information about the investigational biologic product is submitted to the FDA in the form of a BLA requesting approval to market the product for one or more indications. ATYR1923 and our other potential product candidates are proteins that will be regulated as biological products subject to the BLA marketing pathway. Under federal law, the submission of most BLAs is subject to an application user fee, and the sponsor of an approved BLA is also subject to an annual prescription drug product program fee. These fees typically increase annually. Applications for orphan drug products are exempted from the BLA user fees, unless the application includes an indication for other than a rare disease or condition.

A BLA 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. FDA approval of a BLA must be obtained before a biologic may be marketed in the United States.

Before approving a BLA, the FDA typically will conduct a pre-approval inspection of 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, the FDA will typically inspect one or more clinical sites to assure compliance with GCP.

Additionally, the FDA may refer any NDA or BLA, including applications for novel biologic candidates which present difficult questions of safety or efficacy, to an advisory committee. 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*

The FDA evaluates a BLA to determine whether the data demonstrate that the biologic is safe, pure, and potent, or effective. After the FDA evaluates the BLA and conducts inspections of manufacturing facilities where the product will be produced, it may issue an approval letter or a Complete Response Letter (CRL). An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. A CRL indicates that the review cycle of the application is complete and the application is not ready for approval. A CRL generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. A CRL 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 with the submission of this additional information, however, the FDA may ultimately decide that the BLA does not satisfy the criteria for approval and issue a denial.

The FDA could also approve the BLA with a Risk Evaluation and Mitigation Strategy (REMS) plan to mitigate risks associated with the product, 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 may also 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 NDAs and BLAs. For example, fast track designation may be granted to a drug or biologic 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 by providing a therapy where none exists or a therapy that may be potentially superior to existing therapy based on efficacy or safety factors. The key benefits of fast track designation are more frequent interactions with the FDA during development and testing and eligibility for priority review. The FDA may also review sections of the NDA or BLA for a fast track product on a rolling basis before the complete application is submitted, if the sponsor and the FDA agree on a schedule for the submission of the application sections, and the sponsor pays any required user fees upon submission of the first section of the application. Based on results of the Phase 3 clinical trial(s) submitted in a BLA, the FDA may grant the BLA 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. Fast track designation may be withdrawn by the sponsor or rescinded by the FDA if the designation is no longer supported by data emerging in the clinical trial process.

Under the accelerated approval program, the FDA may approve a BLA 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. Drugs and biologics granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval. 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, 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 and for which there is no reasonable expectation that the cost of developing and making a drug for this type of disease or condition will be recovered from sales in the United States. Orphan drug designation must be requested before submitting an NDA or BLA. After the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA.

Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process, but it 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. Orphan drug exclusivity, however, also could block the approval of one of our products for seven years if a competitor obtains approval of the same drug as defined by the FDA for treatment of the same indication or disease.

#### *Pediatric Trials and Exclusivity*

Under the Pediatric Research Equity Act of 2003, as amended (PREA), BLAs or supplement to a BLA must contain data that are adequate to assess the safety and effectiveness of an investigational drug or biologic 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 (PSP) within sixty days of an end-of-phase 2 meeting or, if there is no such meeting, as early as practicable before the initiation of the Phase 3 or Phase 2/3 clinical trial. 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 or biologic for an indication for which orphan designation has been granted, except under certain circumstances.

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 orphan exclusivity. This six-month exclusivity may be granted if a BLA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data.

#### ***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 EU, for example, a clinical trial authorization application (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 GCP the applicable regulatory requirements, and the ethical principles that have their origin in the Declaration of Helsinki.

### ***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. Private payors often follow Centers for Medicine & Medicaid Services (CMS's) determinations relating to Medicare and Medicaid with respect to coverage policy and payment limitations in setting their own reimbursement policies. 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 or sufficient 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 ACA 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. There remains judicial and Congressional challenges to certain aspects of the ACA, as well as efforts by the Trump administration to repeal or replace certain aspects of the ACA. While Congress has not passed comprehensive repeal legislation, it has enacted laws that modify certain provisions of the ACA. For example, the Bipartisan Budget Act of 2018 (the BBA), among other things, amended the ACA, 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 included 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 June 14, 2018, U.S. Court of Appeals for the Federal Circuit ruled that the federal government was not required to pay more than \$12.0 billion in ACA risk corridor payments to third-party payors who argued were owed to them. This case has been subsequently appealed to the U.S. Supreme Court. On December 14, 2018, a U.S. District Court Judge in the Northern District of Texas (Texas District Court Judge), ruled that the individual mandate is a critical and inseparable feature of the ACA, and therefore, because it was repealed as part of the Tax Cuts and JOBS Act of 2017, the remaining provisions of the ACA are invalid as well. On December 18, 2019, the U.S. Court of Appeals for the 5th Circuit ruled that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the ACA are invalid as well. In December 2018, the CMS published a final rule permitting further collections and payments to and from certain ACA qualified health plans and health insurance issuers under the ACA risk adjustment program in response to the outcome of federal district court litigation regarding the method CMS uses to determine this risk adjustment. In addition, the 2020 federal spending package permanently eliminates, effective January 1, 2020, the ACA-mandated "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminates the health insurer tax. Further, on January 20, 2017, President Trump signed an Executive Order directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA 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 additional legislation to modify, repeal, or replace elements of the ACA that are repealed. Thus, the full impact of the ACA, 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.

Additionally, the Trump administration's budget proposal for fiscal year 2020 contained further drug price control measures that could be enacted during the 2020 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. Additionally, the Trump administration released a "Blueprint" to lower drug prices and reduce out of pocket costs of drugs that contains additional proposals to increase manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products and reduce the out of pocket costs of drug products paid by consumers. The U.S. Department of Health and Human Services (HHS) has solicited feedback on some of these measures and has implemented others under its existing authority. For example, in May 2019, CMS issued a final rule to allow Medicare Advantage Plans the option of using step therapy for Part B drugs beginning January 1, 2020. This final rule codified CMS's policy change that was effective January 1, 2019. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

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 (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 ACA referred to as the federal Physician Payments Sunshine Act, that requires drug and biologics manufacturers to disclose payments and other transfers of value provided to physicians (as defined by the law) 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 (HITECH) and its implementing regulations, which imposes certain requirements on HIPAA covered entities and their business associates 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 transparency, marketing and drug pricing reporting, and 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 ACA 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 ACA 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 (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 significant civil and criminal penalties, exclusion from participation in government healthcare programs, such as Medicare and Medicaid and imprisonment, disgorgement, damages, fines, additional reporting requirements and regulatory oversight 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 December 31, 2019, we had 44 employees, 39 of which were full-time employees. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

### **Financial Information about Segments**

We operate in a single accounting segment. Refer to Note 1 to our consolidated financial statements included elsewhere in this Annual Report.

### **Emerging Growth Company Status**

Under the Jumpstart Our Business Startups Act of 2012 (JOBS Act), we qualify as an emerging growth company. Emerging growth companies can delay adopting new or revised accounting standards until such time as those standards apply to private companies. We have irrevocably elected not to avail ourselves of this exemption 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. We could be an emerging growth company up to December 31, 2020, although circumstances could cause us to lose that status earlier.

### **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](http://www.atyrpharma.com).

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. Our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, and amendments to these reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act, are available free of charge on our website as soon as reasonably practicable after such reports and amendments are electronically filed with, or furnished to, the SEC. You may obtain copies of these reports directly from us or from the SEC. In addition, the SEC maintains information for electronic filers (including aTyr Pharma, Inc.) at its website at [www.sec.gov](http://www.sec.gov). We also make available copies of our news releases and other financial information and updates with respect to our business on our website. 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.

## Item 1A. Risk Factors

*You should carefully consider the following risk factors, as well as the other information in this Annual Report, 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 will need to raise additional capital or enter into strategic partnering relationships to fund our operations.***

The development of therapeutic product candidates is expensive, and we expect our research and development expenses to fluctuate. As of December 31, 2019, our cash, cash equivalents and available-for-sale investments were \$31.1 million. Since that time, we received \$8.0 million related to the Kyorin Agreement and approximately \$20.7 million in gross proceeds from our underwritten follow-on public offering of common stock, before deducting underwriting discounts, commissions and offering expenses payable by us. We believe that our current cash, cash equivalents and available-for-sale investments, will be sufficient to meet our anticipated cash requirements for a period of at least one year from the date of this Annual Report. 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 equity or debt offerings, grant funding, collaborations, strategic partnerships and/or licensing arrangements. 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, preclinical 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 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 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.



We may decide to enter into additional strategic partnerships, including collaborations with pharmaceutical and biotechnology companies, to enhance and accelerate the development and potential commercialization of our product candidates. We face significant competition in seeking appropriate partners, and the negotiation process is time-consuming and complex. Moreover, we may not be successful in our efforts to establish any new strategic partnership or other collaborative arrangement for any of our product candidates and programs for a variety of reasons, including strategic fit with partners and differences in analysis of commercial value and regulatory risk. We may not be able to negotiate strategic partnerships on a timely basis, on acceptable terms or at all. We are unable to predict when, if ever, we will enter into any new strategic partnership because of the numerous risks and uncertainties associated with establishing strategic partnerships. Even if we are successful in our efforts to establish new 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.***

As of December 31, 2019, our term loans (Term Loans) under a loan and security agreement, dated November 18, 2016, as amended (Loan Agreement) among us and Silicon Valley Bank and Solar Capital Ltd. (Lenders) consisted of \$7.3 million principal outstanding to be repaid ratably, on a monthly basis, through November 2020. In addition, we have a \$1.8 million final payment due in the fourth quarter of 2020. 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 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 entered into with the Lenders, we have agreed not to encumber any of the intellectual property of ours or our subsidiaries. As a result, if we default on any of our obligations under the Loan Agreement, the Lenders could foreclose on their security interest and liquidate some or all of the collateral, which would harm our business, financial condition and results of operations and could require us to reduce or cease operations.

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 if we experience a material adverse change. 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 our 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.

***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 consolidated net losses of \$23.8 million, \$34.5 million and \$48.2 million for the years ended December 31, 2019, 2018 and 2017, respectively. As of December 31, 2019, we had an accumulated deficit of \$322.3 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 offerings, grant funding, collaborations, strategic partnerships and/or licensing arrangements. 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 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;
- 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 or NRP2 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.

### **Risks related to the discovery, development and regulation of our product candidates**

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

Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must conduct extensive clinical trials to demonstrate the safety and efficacy of the product candidates in humans. Clinical trials are expensive, time-consuming, often delayed and uncertain as to outcome. We cannot guarantee that our ATYR1923 Phase 1b/2a clinical trial in patients with pulmonary sarcoidosis, or future trials we may plan to conduct, will be initiated or conducted as planned or completed on schedule, if at all. 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:

- our 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 CROs and clinical trial sites;
- delays in obtaining required institutional review board (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 at any time before or during a clinical trial, including 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 (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 a 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, we may need to conduct additional studies to bridge our modified product candidates to earlier versions.

If the results of our clinical trials, including our ongoing ATYR1923 Phase 1b/2a clinical trial in patients with pulmonary sarcoidosis, 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 (REMS); be subject to litigation; or experience damage to our reputation.

To date, the safety and efficacy of ATYR1923 in humans has not been studied to a significant extent. Accordingly, ATYR1923 and future 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.

***Interim, top-line and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.***

From time to time, we may publicly disclose preliminary or top-line data from our clinical studies, which are based on a preliminary analysis of then-available data, and the results and related findings and conclusions are subject to change following a more comprehensive review of the data related to the particular study or trial. We also make assumptions, estimations, calculations and conclusions as part of our analyses of data, and we may not have received or had the opportunity to fully and carefully evaluate all data. As a result, the top-line results that we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. Top-line data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, top-line data should be viewed with caution until the final data are available. From time to time, we may also disclose interim data from our clinical studies.

In addition, we may report interim analyses of only certain endpoints rather than all endpoints. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. For example, we recently announced results from a blinded interim analysis of safety and tolerability, the primary endpoint of our ongoing Phase 1b/2a clinical trial. These results may not be consistent with final data for this trial. Adverse differences between preliminary or interim data and final data could significantly harm our business prospects. Further, disclosure of interim data by us or by our competitors could result in volatility in the price of our common stock.

Further, others, including regulatory agencies, may not accept or agree with our assumptions, estimates, calculations, conclusions or analyses or may interpret or weigh the importance of data differently, which could impact the value of the particular program, the approvability or commercialization of a particular product candidate or product and our company in general. In addition, the information we choose to publicly disclose regarding a particular study or clinical trial is based on what is typically extensive information, and you or others may not agree with what we determine is material or otherwise appropriate information to include in our disclosure, and any information we determine not to disclose may ultimately be deemed significant with respect to future decisions, conclusions, views, activities or otherwise regarding a particular product, product candidate or our business. If the top-line data that we report differ from actual results, or if others, including regulatory authorities, disagree with the conclusions reached, our ability to obtain approval for, and commercialize, our product candidates may be harmed, which could harm our business, operating results, prospects or financial condition.

***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, including ATYR1923, 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 extracellular proteins derived from the HARS family (Resokine pathway) and NRP2 biology, 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 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. For example, we are currently evaluating ATYR1923 in a Phase 1b/2a clinical trial in patients with pulmonary sarcoidosis. While estimates of pulmonary sarcoidosis prevalence vary, we estimate that pulmonary sarcoidosis affects an estimated 200,000 patients in the United States. Of that population, however, we estimate that approximately 30% experience progressive disease such that our targeted population is significantly smaller. The eligibility criteria for our clinical trials may further limit the pool of available participants in our trials. In particular, for our ATYR1923 Phase 1b/2a trial, patients must, among other criteria: (i) have a biopsy-proven diagnosis of pulmonary sarcoidosis for a defined period of time; (ii) have symptomatic or active disease based on pulmonary function test, dyspnea evaluation and FDG-PET scan; and (iii) be on a stable dose of steroids at a certain dosage. 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, limitations required by trial protocols or other reasons.

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, including our ATYR1923 Phase 1b/2a clinical trial in patients with pulmonary sarcoidosis, 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 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.

***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 the bulk of our research and development efforts to date on studying extracellular functions of tRNA synthetase biology, a newly discovered area of biology. We have also identified NRP2, as a receptor for ATYR1923 and have focused research efforts on NRP2 biology. Our future success is highly dependent on the successful development of product candidates based these new areas of biology, including ATYR1923 and additional product candidates arising from the Resokine pathway or other pathways. Extracellular tRNA synthetase-based biology and NRP2 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 immunomodulation 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 represents a new therapeutic approach, developing and commercializing our product candidates, including ATYR1923, 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 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 cGMPs and related requirements, with a cost of goods that allows for an attractive return on investment;
- obtaining and maintaining third-party coverage and adequate reimbursement of our product candidates;
- 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 immunomodulatory 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 preclinical observations may prove to be incorrect, and the data generated in animal models or observed in limited patient populations may be of limited value, and may not be applicable in clinical trials conducted under the controlled conditions required by applicable regulatory requirements and our protocols. For example, we have not extensively studied the activity of the Resokine pathway in patients with ILDs, which forms the basis for our ongoing clinical trial of ATYR1923 in patients with pulmonary sarcoidosis.

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 iMod domain may not be substantiated in other animal models or in clinical trials. Further, based on the discovery of the involvement of NRP2 in the mechanism of action of ATYR1923, we are still expanding our knowledge of the role of the NRP2 pathway, and in particular how the Resokine pathway modulates disease pathology. 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.

***We have previously conducted and we may conduct additional clinical trials of ATYR1923 outside of the United States. The FDA, however, may not accept data from such trials, in which case our development plans will be delayed, which could materially harm our business.***

In June 2018, we completed a Phase 1 clinical trial of ATYR1923 in healthy subjects in Australia. This randomized, double-blind, placebo-controlled study investigated the safety, tolerability, immunogenicity, and PK of intravenous ATYR1923 in 36 healthy volunteers. In addition, we may choose to conduct additional clinical trials for ATYR1923 in countries outside the United States, subject to applicable regulatory approval.

Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of such study data is generally subject to certain conditions. For example, in cases where data from foreign clinical trials are intended to serve as the basis for marketing approval in the United States, the FDA will generally not approve the application on the basis of foreign data alone unless (i) the data are applicable in the U.S. population and U.S. medical practice; and (ii) the trials were performed by clinical investigators of recognized competence and pursuant to GCP regulations. Additionally, the FDA's clinical trial requirements, including sufficient size of patient populations and statistical powering, must be met. In addition, when studies are conducted only at sites outside of the United States, the FDA generally does not provide advance comment on the clinical protocols for the studies, and therefore there is an additional risk that the FDA could determine that the study design or protocol for a non-U.S. clinical trial was inadequate, which would likely require us to conduct additional clinical trials, in which case our development plans will be delayed, which could materially harm our business.

Conducting clinical trials outside the United States also exposes us to additional risks, including risks associated with:

- additional foreign regulatory requirements;
- foreign exchange fluctuations;
- compliance with foreign manufacturing, customs, shipment and storage requirements;
- cultural differences in medical practice and clinical research; and
- diminished protection of intellectual property in some countries.

***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 our first clinical trial candidate, ATYR1940, completed in 2016 and 2017, we observed low levels of antibodies to ATYR1940 in some subjects in response to the administration of ATYR1940. Although these antibody observations were without associated clinical symptoms, the development of higher levels of such antibodies over a longer course of treatment may ultimately limit efficacy 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 (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 our ongoing Phase 1b/2a clinical trial of ATYR1923 or 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, including ATYR1923. 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 expand applications of ATYR1923 to additional immune-mediated diseases and leverage our discovery engine to identify the therapeutic potential of NRP2 biology and extracellular proteins derived from tRNA synthetases to help identify or discover additional product candidates. 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 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 contract 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 biological license application (BLA) on a timely basis and must adhere to the FDA's Good Laboratory Practices (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 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 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. 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 immuno-modulatory 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, fusion proteins, such as ATYR1923, include an additional antibody domain to improve 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. 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 or expires, 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.

***We may not receive orphan drug designation for our product candidates under any 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.***

We may apply for orphan drug designation for our product candidates. Orphan drug status confers up to ten years of marketing exclusivity in Europe, and up to seven years of marketing exclusivity in the United States, for a particular product that is the first to obtain approval in a specified indication. 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.***

We may seek, from time to time, breakthrough therapy or fast track designation for our 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 preclinical 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 if we receive breakthrough therapy or fast track designation, 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 CDMOs will be subject to continual review and inspections to assess compliance with cGMP and adherence to commitments made in any BLA or marketing authorization application (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 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 CDMOs' 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 depend on our collaborations with Kyorin and CSL and may depend on collaborations with additional third parties for the development and commercialization of certain of our product candidates. If our collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates.***

We have entered into, and may continue to enter into, research collaborations for the research and development of specified product candidates. Our sole source of revenue depends upon the performance by these collaborators of their responsibilities under these arrangements. For example, we recently entered into a license agreement with Kyorin for the development and commercialization of ATYR1923 for ILDs in Japan pursuant to which we received an \$8.0 million upfront payment. We are also eligible to receive up to an additional \$167.0 million in the aggregate upon achievement of certain development, regulatory and sales milestones, as well as tiered royalties ranging from the mid-single digits to mid-teens on net sales in Japan. We previously entered into a research collaboration agreement with CSL related to the development of product candidates derived from up to four tRNA synthetases where CSL funds research and development activities and may be obligated to pay a total of \$4.25 million per synthetase program in option fees based on achievement of research milestones and CSL's determination to continue development. The development efforts of our collaborators are subject to the same risks and uncertainties described above with respect to our independently developed product candidates.

Some collaborators may not succeed in their product development efforts. It is possible that our collaborators may be unable to obtain regulatory approval of our product candidates or successfully market and commercialize any such products for which regulatory approval is obtained. Other collaborators may not devote sufficient time or resources to the programs covered by these arrangements, and we may have limited or no control over the time or resources allocated by these collaborators to these programs. The occurrence of any of these events may cause us to derive little or no revenue from these arrangements, lose opportunities to validate our product candidates, or force us to curtail or cease our development efforts in these areas.

Our collaborators may breach or terminate their agreements with us, including termination without cause at subject to certain prior written notice requirements, and we may be unsuccessful in entering into and maintaining other collaborative arrangements for the development of product candidates. For example, following the first anniversary of the effective date of the Kyorin Agreement, Kyorin has the right to terminate the agreement for any reason upon 90 days advance written notice to us. Under the CSL Agreement, CSL has sole discretion to proceed to the next research phase for any synthetase program and there can be no assurance that CSL will elect to negotiate a license agreement with us for any IND candidates that result from the research collaboration. In addition, if we are unable to maintain existing collaboration arrangements or enter into new ones, our ability to generate licensing, milestone or royalty revenues would be materially impaired.

***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 submissions and approval of our product candidates.

***We rely and intend to rely on third parties to produce preclinical, clinical and commercial supplies of our product candidates.***

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

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

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

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

We currently rely on a single CDMO for process development and scale-up of ATYR1923, including the manufacture of bulk drug substance for our projected needs for initial clinical trials. 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 preclinical 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 both industry and 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 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.

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. 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 *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.

***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 (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, product candidates or 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 business could be adversely affected by the effects of health epidemics, including the recent COVID-19 outbreak, in regions where we or third parties on which we rely have concentrations of clinical trial sites, significant manufacturing facilities or other business operations.***

Our business could be adversely affected by health epidemics, including COVID-19, in regions where we or third parties on which we rely have concentrations of clinical trial sites, significant manufacturing facilities or other business operations.

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

Our ongoing ATYR1923 Phase 1b/2a clinical trial in patients with pulmonary sarcoidosis will be affected by the COVID-19 outbreak. In particular, patient enrollment and participation may be difficult or delayed. According to the Centers for Disease Control and Prevention, people who have serious chronic medical conditions, including lung disease, are at higher risk of getting very sick from COVID-19. As a result, current or potential patients in our ongoing Phase 1b/2a clinical trial may choose to not enroll, not participate in follow-up clinical visits or drop out of the trial as a precaution against contracting COVID-19. Further, some patients may not be able to comply with clinical trial protocols if quarantines impede patient movement or interrupts healthcare services. While the trial continues to progress, as a result of the recent COVID-19 outbreak in the United States, many clinical trial sites in our ongoing Phase 1b/2a clinical trial have temporarily suspended dosing of previously-enrolled patients and/or enrollment of new patients. As a result, we anticipate that the availability of top-line results from the clinical trial will be delayed. We are in close contact with our clinical trial sites as we assess and attempt to mitigate the impact of COVID-19 on our clinical trial, including the scope of any delays. Any of these events could significantly delay our Phase 1b/2a clinical trial, increase the cost of completing our Phase 1b/2a clinical trial and lead to questions about the integrity, reliability or robustness of the data from our Phase 1b/2a clinical trial.

In addition, under the terms of the Kyorin Agreement, we rely on Kyorin to fund all research, development, regulatory, marketing and commercialization activities in Japan, as well as support our global development efforts for ATYR1923. If Kyorin's operations are limited due to the COVID-19 outbreak in Japan or in other regions where Kyorin operates or relies on third party operations, the development of ATYR1923 in Japan or globally may be significantly delayed and adversely affected, which may in turn delay or limit our receipt of any additional payments under the Kyorin Agreement.

Further, we currently rely, and expect to continue to rely, on third parties to conduct some or all aspects of product manufacturing, protocol development, and research and preclinical and clinical testing with respect to our product candidates. While many materials on

which we rely may be obtained by more than one supplier, port closures, travel bans and other restrictions resulting from the COVID-19 outbreak may disrupt our supply chain or limit our ability to obtain sufficient materials to conduct our operations.

As a result of these events and uncertainties, we may need to obtain additional funding through a combination of equity offerings, grant funding, collaborations, strategic partnerships and/or licensing arrangements, and potentially through debt financings, if available on acceptable terms or at all. We may be unable to raise additional funds on acceptable terms or at all. The impact of COVID-19 on capital markets may affect the availability, amount and type of financing available to us in the future. If we are unable to raise additional funds, 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.

The ultimate impact of the COVID-19 outbreak or a similar health epidemic is highly uncertain and subject to change. We do not yet know the full extent of potential delays or impacts on our business, the business of third parties on which we rely, our clinical trials, healthcare systems or the global economy as a whole. These effects could have a material impact on our operations.

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

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

***We may undertake internal restructuring activities in the future that could result in disruptions to our business or otherwise materially harm our results of operations or financial condition.***

From time to time we may undertake internal restructuring activities as we continue to evaluate and attempt to optimize our cost and operating structure in light of developments in our business strategy and long-term operating plans. For example, we implemented a corporate restructuring and program prioritization plan in May 2018 that included a reduction in our workforce. Any such restructuring activities may result in write-offs or other restructuring charges. There can be no assurance that any restructuring activities that we have undertaken or undertake in the future will achieve the cost savings, operating efficiencies or other benefits that we may initially expect. Restructuring activities may also result in a loss of continuity, accumulated knowledge and inefficiency during transitional periods and thereafter. In addition, internal restructurings can require a significant amount of time and focus from management and other employees, which may divert attention from commercial operations. If any internal restructuring activities we have undertaken or undertake in the future fail to achieve some or all of the expected benefits therefrom, our business, results of operations and financial condition could be materially and adversely affected.

***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 Pangu BioPharma, in collaboration with the Hong Kong University of Science and Technology. Additionally, we have conducted clinical trials in the European Union (EU) 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 \$10.0 million per occurrence and up to \$10.0 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 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, there can be no assurance that this will be successful in preventing violations of anti-corruption laws. If we are not in compliance with anti-corruption laws and other laws governing the conduct of business with government entities (including local laws), we may be subject to criminal and civil penalties and other remedial measures, which could harm our reputation and have a material adverse impact on our business, financial condition, results of operations and prospects. Any investigation of any actual or alleged violations of such laws could also harm our reputation or have an adverse impact on our business, prospects, financial condition and results of operations.

***Our business and operations would suffer in the event of system failures.***

We utilize information technology systems and networks to process, transmit and store electronic information in connection with our business activities. As use of digital technologies has increased, cyber incidents, including deliberate attacks and attempts to gain unauthorized access to computer systems and networks, which could result in the theft of our intellectual property, have increased in frequency and sophistication. These threats pose a risk to the security of our systems and networks and the confidentiality, availability and integrity of our data. There can be no assurance that we will be successful in preventing cyber-attacks or mitigating their effects.

Despite the implementation of security measures, our internal computer systems and those of our contractors and consultants are vulnerable to damage from such cyber-attacks, including computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Such an event could cause interruption of our operations. For example, the loss of data from completed clinical trials for our product candidates could result in delays in our regulatory approval efforts and significantly increase our costs. Additionally, theft of our intellectual property or proprietary business information could require substantial expenditures to remedy. To the extent that any disruption or security breach were to result in a loss of or damage to our data, theft of our intellectual property, or inappropriate disclosure of confidential or proprietary information, we could suffer reputational harm or face litigation or adverse regulatory action and the development of our product candidates could be delayed.

***We may be subject to certain regulations, including federal and state healthcare fraud and abuse laws and health information privacy and security laws. Any failure to comply with these regulations could have a material adverse effect on our business and financial condition.***

If we obtain FDA approval for any of our product candidates and begin commercializing those products in the United States, our operations may be subject to various federal and state healthcare laws, including, without limitation, fraud and abuse laws, including false claims and anti-kickback laws, data privacy and security laws, including the Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act, as well as transparency laws regarding payments or other items of value provided to healthcare providers. These laws may impact, among other things, our research, 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. It is possible that some of our business activities could be subject to challenge under one or more of these laws. 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 significant administrative civil and criminal penalties, damages, fines, disgorgement, imprisonment, possible exclusion from participation in Medicare, Medicaid and other federal

healthcare programs, additional reporting requirements and regulatory oversight 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.

In addition, as of May 25, 2018, the General Data Protection Regulation (GDPR), regulates the collection and use of personal data in the EU. The GDPR covers any business, regardless of its location, that provides goods or services to residents in the EU and, thus, could incorporate our activities in EU member states. The GDPR imposes strict requirements on controllers and processors of personal data, including special protections for “sensitive information,” which includes health and genetic information of individuals residing in the EU. The GDPR grants individuals the opportunity to object to the processing of their personal information, allows them to request deletion of personal information in certain circumstances, and provides the individual with an express right to seek legal remedies in the event the individual believes his or her rights have been violated. Further, the GDPR imposes strict rules on the transfer of personal data out of the EU to regions that have not been deemed to offer “adequate” privacy protections, such as the U.S. currently. Failure to comply with the requirements of the GDPR and related national data protection laws of the EU member states, which may deviate slightly from the GDPR, may result in warning letters, mandatory audits and financial penalties, including fines of up to 4% of global revenues, or €20,000,000, whichever is greater. As a result of the implementation of the GDPR, we may be required to put in place additional mechanisms ensuring compliance with the new data protection rules.

Further, there is significant uncertainty related to the manner in which data protection authorities will seek to enforce compliance with GDPR. For example, it is unclear whether the authorities will conduct random audits of companies doing business in the EU, or act solely after complaints are filed claiming a violation of the GDPR. The lack of compliance standards and precedent, enforcement uncertainty and the costs associated with ensuring GDPR compliance may be onerous and adversely affect our business, financial condition, results of operations and prospects.

In addition, California recently enacted the California Consumer Privacy Act (CCPA), which creates new individual privacy rights for California consumers (as defined in the law) and places increased privacy and security obligations on entities handling certain personal data of consumers or households. The CCPA requires covered companies to provide new disclosure to consumers about such companies’ data collection, use and sharing practices, provide such consumers new ways to opt-out of certain sales or transfers of personal information, and provide consumers with additional causes of action. The CCPA went into effect on January 1, 2020, and the California Attorney General may bring enforcement actions for violations beginning July 1, 2020. The CCPA was amended on September 23, 2018, and it remains unclear what, if any, further modifications will be made to this legislation or how it will be interpreted. As currently written, the CCPA may impact our business activities and exemplifies the vulnerability of our business to the evolving regulatory environment related to personal data and protected health information.

***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 EU that the U.K. will exit the EU (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 CDMOs, 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 conducted our Phase I clinical trial for ATYR1923 in Australia and sponsor research in Hong Kong. Our current ATYR1923 Phase 1b/2a trial is being conducted in sites across the United States and may expand to sites in Europe. 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 CDMOs 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 CDMOs are unable to scale the manufacturing process to produce commercial quantities of our product candidates, or our CDMOs do not pass required regulatory pre-approval inspections, our commercialization efforts will be harmed.

In addition, any significant disruption in our relationships with our CDMOs 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 CDMOs 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. Although we believe we are the only company engaged in the discovery and development of therapeutics based on novel functions of tRNA synthetases and NRP2 biology, we are aware of other companies that could compete with our product candidate, ATYR1923 for the treatment of pulmonary sarcoidosis and other ILDs.

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 product candidate or future product candidates 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 Medicine & Medicaid Services (CMS), 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. For example, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010 (collectively, the ACA) was passed in March 2010, and substantially changed the way healthcare is financed by both governmental and private insurers, and continues to significantly impact the U.S. pharmaceutical industry. There remain judicial and congressional challenges to certain aspects of the ACA, as well as recent efforts by the Trump administration to repeal or replace certain aspects of the ACA. While Congress has not passed comprehensive repeal legislation, it has enacted laws that modify certain provisions of the ACA such as removing penalties, starting January 1, 2019, for not complying with the ACA's individual mandate to carry health insurance. In addition, the 2020 federal spending package permanently eliminates, effective January 1, 2020, the ACA-mandated "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminates the health insurer tax. On December 14, 2018, a Texas U.S. District Court Judge ruled that the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress as part of the Tax Cuts and Jobs Act of 2017. Additionally, on December 18, 2019, the U.S. Court of Appeals for the 5th Circuit ruled that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the ACA are invalid as well. It is unclear how this decision, future decisions, subsequent appeals, and other efforts to repeal and replace the ACA will impact the ACA and our business. In addition, there has been heightened governmental scrutiny in the United States of pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. 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 ACA. 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. If coverage and reimbursement is available only to limited levels, we may not be able to successfully commercialize our product candidates for which we obtain marketing approval. As a result, we may have difficulty raising capital 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 historically has been highly volatile and is likely to continue to be volatile, and you could lose all or part of your investment.***

The market price of our common stock has been volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. In addition to the factors discussed in this "Risk Factors" section and elsewhere in this report, these factors include:

- 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 an IND or BLA for any of our product candidates and any adverse development or perceived adverse development with respect to the FDA's review of that IND or BLA;
- failure of our strategic partners to perform under our collaborations or early termination of collaborations;
- failure to successfully develop and commercialize our product candidates;
- limited market sizes and 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 current or 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 biopharmaceutical 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 issue an adverse or misleading opinion regarding our common stock;
- changes in the market valuations of similar companies;
- changes in the structure of healthcare payment systems;
- general market or macroeconomic conditions;
- sales of our common stock by us or our stockholders in the future;
- a potential additional reverse stock split if we are unable to maintain a stock price above \$1.00 per share of common stock; and
- trading volume of our common stock.

In addition, companies trading in the stock market in general, and on the Nasdaq Capital 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.

***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 as well as rules subsequently implemented by the SEC and The Nasdaq Stock Market have imposed various requirements on public companies. In July 2010, the Dodd-Frank Wall Street Reform and Consumer Protection Act (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 initial public offering (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.

***Our executive officers, directors, 5% holders and their affiliates currently 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 19, 2020, based on the latest information available to us, our executive officers, directors, holders known by us to own 5% of our voting stock and their affiliates own approximately 25.01% of our voting stock. One of our principal stockholders owns all shares of our outstanding non-voting convertible preferred stock, which, if converted, would further increase the percentage of our voting stock held by our executive officers, directors, holders known by us to own 5% of our voting stock and their affiliates. Therefore, our executive officers, directors, holders known by us to own 5% of our voting stock 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 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 up to December 31, 2020, 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 \$1.0 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 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, grant funding, collaborations, strategic partnerships and/or licensing arrangements. For example, in February 2020, we completed an underwritten follow-on public offering of 4,235,294 shares of our common stock at a price to the public of \$4.25 per share and in March 2020, the underwriters fully exercised their over-allotment option for the issuance of an additional 635,294 shares of common stock which resulted in total offering gross proceeds of approximately \$20.7 million, before deducting underwriting discounts, commissions and offering expenses payable by us. 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.

Additionally, in May 2019, we entered into a sales agreement with H.C. Wainwright & Co., LLC (Wainwright) for an at-the-market offerings program (ATM Offering Program) under which we may offer and sell shares of our common stock having an aggregate offering price of up to \$10.0 million. Wainwright is entitled to a commission at a fixed commission rate equal to 3% of the gross proceeds. Under the ATM Offering Program with Wainwright, as of December 31, 2019, we had sold an aggregate of 611,687 shares of common stock at an average price of \$5.43 per common share for net proceeds of approximately \$3.0 million.

In addition, sales of a substantial number of shares of our common stock by our existing stockholders in the public market or the perception that these sales might occur, could depress the market price of our common stock and could impair our ability to raise capital through the sale of additional equity securities. 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 or plan to register all common stock that we may issue under our employee benefits plans as well as shares of common stock underlying options to purchase shares of our common stock that were granted as inducement grants. As a result, once registered, 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 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 relies in part on the research and reports that industry or financial analysts publish about us or our business. If no or few analysts commence coverage or continue coverage of us, the trading price of our stock would likely decrease. 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. For example, in 2018 three analysts ceased to cover our stock and in 2019, one analyst ceased to cover our stock and coverage by a bank was suspended when an analyst changed employment.

***We could be subject to securities class action litigation.***

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

***We may not be able to comply with all applicable listing requirements or standards of the Nasdaq Capital Market and Nasdaq could delist our common stock.***

Our common stock is currently listed on the Nasdaq Capital Market. In order to maintain that listing, we must satisfy minimum financial and other continued listing requirements and standards. One such requirement is that we maintain a minimum bid price of at least \$1.00 per share for our common stock. For example, in August 2018, we received a letter from the Listing Qualifications Department of the Nasdaq Stock Market (Nasdaq) advising us that for 30 consecutive trading days preceding the date of the Notice, the bid price of our common stock had closed below the \$1.00 per share minimum required for continued listing on The Nasdaq Global Select Market pursuant to Nasdaq Listing Rule 5450(a)(1) (the Minimum Bid Price Requirement).

In February 2019, we transferred the listing of our common stock from the Nasdaq Global Select Market to the Nasdaq Capital Market. On June 28, 2019, we filed a Certificate of Amendment to our Restated Certificate of Incorporation with the Secretary of State of the State of Delaware to effect a 1-for-14 reverse stock split of our issued and outstanding common stock. The reverse stock split became effective at 5:00 p.m. Eastern Time on June 28, 2019 and our common stock began trading on a split-adjusted basis on The Nasdaq Capital Market on July 1, 2019.

On July 16, 2019, we were notified by Nasdaq that as of July 15, 2019 we had maintained a closing bid above \$1.00 for a period of 10 consecutive trading days and therefore had regained compliance with the Minimum Bid Price Requirement. There can be no assurance that we will continue to be in compliance with the \$1.00 minimum bid price requirement or comply with Nasdaq's other continued listing standards in the future.

If in the future we are not able to maintain compliance with the Minimum Bid Price Requirement within an allotted grace period, our shares of common stock would be subject to delisting. In the event that our common stock is not eligible for continued listing on Nasdaq or another national securities exchange, trading of our common stock could be conducted in the over-the-counter market or on an electronic bulletin board established for unlisted securities such as the Pink Sheets or the OTC Bulletin Board. In such event, it could become more difficult to dispose of, or obtain accurate price quotations for, our common stock, and there would likely also be a reduction in our coverage by security analysts and the news media, which could cause the price of our common stock to decline further. Also, it may be difficult for us to raise additional capital if we are not listed on a major exchange.

***We have broad discretion in the use of our cash, cash equivalents and investments and are exposed to risks related to the marketable securities we may purchase.***

We have considerable discretion in the application of our existing cash, cash equivalents and investments. 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 certain short-term investments, including but not limited to investment-grade, interest-bearing securities. Historically, investment in these securities has been highly liquid and has experienced only very limited defaults. However, volatility in the financial markets in recent years has created additional uncertainty regarding the liquidity and safety of these investments. Additionally, we may use these proceeds for purposes that do not yield a significant return or any return at all for our stockholders.

***Our ability to use our net operating losses to offset future taxable income may be subject to certain limitations.***

As of December 31, 2019, we had federal net operating loss carryforwards (NOLs) of approximately \$163.7 million, with \$51.2 million of NOLs generated after December 31, 2018 carrying forward indefinitely and \$112.5 million of NOLs that will begin to expire in 2025. We had state NOLs carryforwards of approximately \$163.3 million that will begin to expire in 2021. A lack of future taxable

income would adversely affect our ability to utilize certain of these NOLs before they expire. Unused losses generated in taxable years ending after December 31, 2017 will not expire and may be carried forward indefinitely, but will be deductible only to the extent of 80% of current year taxable income (computed without regard to the deduction for the NOLs) in any given year. It is uncertain if and to what extent various states will conform to the newly enacted federal tax law.

In general, under Section 382 of the Internal Revenue Code of 1986, as amended, or the Code, a corporation that undergoes an “ownership change” (as defined under Section 382 of the Code and applicable Treasury Regulations) is subject to limitations on its ability to utilize its pre-change NOLs to offset future taxable income. We have experienced ownership changes in the past, and may experience a future ownership change (including, potentially, in connection with this offering), under Section 382 of the Code that could affect our ability to utilize the NOLs to offset our income. Furthermore, our ability to utilize NOLs of companies that we have acquired or may acquire in the future may be subject to limitations. There is also a risk that due to regulatory changes, such as suspensions on the use of NOLs or other unforeseen reasons, our existing NOLs could expire or otherwise be unavailable to reduce future income tax liabilities, including for state tax purposes. For these reasons, we may not be able to utilize a material portion of the NOLs reflected on our balance sheet, even if we attain profitability, which could potentially result in increased future tax liability to us and could adversely affect our operating results and financial condition.

***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.

In addition, pursuant to the Loan Agreement, we are restricted from paying cash dividends without the consent of the Lenders and future debt instruments may materially restrict our ability to pay dividends on our common stock. Any future determination related to 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, tax considerations, legal or contractual restrictions, business prospects, the requirements of current or then-existing debt instruments, general economic conditions and other factors our board of directors may deem relevant.

***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.

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

Our amended and restated bylaws provide that the Court of Chancery of the State of Delaware will be the sole and exclusive forum for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or employees to our company or our stockholders, (iii) any action asserting a claim against our company arising pursuant to any provision of the Delaware General Corporation Law or our amended and restated certificate of incorporation or bylaws, or (iv) any action asserting a claim against our company governed by the internal affairs doctrine. This choice of forum provision does not apply to suits brought to enforce a duty or liability created by the Securities Act or the Exchange Act, or any other claim for which the federal courts have exclusive jurisdiction.

This choice of forum provision may limit a stockholder's ability to bring certain claims in a judicial forum that it finds favorable for disputes with us or any of our directors, officers, other employees or stockholders, which may discourage lawsuits with respect to such claims, although our stockholders will not be deemed to have waived our compliance with federal securities laws and the rules and regulations thereunder. If a court were to find this choice of forum provision to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could adversely affect our business and financial condition.

**Item 1B. Unresolved Staff Comments.**

Not applicable.

**Item 2. Properties.**

We lease our headquarters located at 3545 John Hopkins Court, Suite #250, San Diego, California pursuant to a lease agreement that expires on May 15, 2023. The lease covers 20,508 rentable square feet of office and laboratory space. 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 Disclosures.**

Not applicable.

**PART II**

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

**Market Information**

Our common stock is traded on the Nasdaq Capital Market under the symbol "LIFE".

## Holders of Record

As of March 19, 2020, there were approximately 43 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. In addition, pursuant to our Loan Agreement, we are restricted from paying cash dividends without the consent of the lenders and future debt instruments may materially restrict our ability to pay dividends on our common stock. 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, tax considerations, legal or contractual restrictions, business prospects, the requirements of current or then-existing debt instruments, general economic conditions 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.

## Recent Sales of Unregistered Securities

During the year ended December 31, 2019, 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, 2019.

## 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. Amounts are in thousands, except per share amounts.

	Years Ended December 31,		
	2019	2018	2017
<b>Statements of Operations Data:</b>			
Loss from operations	\$ (22,978)	\$ (32,820)	\$ (47,145)
Consolidated net loss	(23,763)	(34,515)	(48,207)
Net loss attributable to aTyr Pharma, Inc.	(23,603)	(34,515)	(48,207)
Comprehensive loss	(23,743)	(34,455)	(48,251)
Comprehensive loss attributable to aTyr Pharma, Inc. common stockholders	(23,583)	(34,455)	(48,251)
Net loss per share attributable to common stock holders, basic and diluted	\$ (7.03)	\$ (16.11)	\$ (26.13)
Weighted average common stock shares outstanding, basic and diluted	3,355,600	2,141,961	1,845,033



	As of December 31,		
	2019	2018	2017
<b>Consolidated Balance Sheet Data:</b>			
Cash, cash equivalents and available-for-sale investments	\$ 31,144	\$ 49,545	\$ 85,119
Total assets	36,188	52,746	89,355
Working capital	19,002	39,970	76,594
Long-term debt, net of current portion and issuance costs and discount	—	8,263	14,719
Accumulated deficit	(322,304)	(298,701)	(264,186)
Total stockholders' equity	21,026	33,650	64,245

## 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. 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 are a biotherapeutics company engaged in the discovery and development of innovative medicines based on novel immunological pathways. We have concentrated our research and development efforts on a newly discovered area of biology, the extracellular functionality and signaling pathways of tRNA synthetases. 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 a potential pipeline of protein compositions derived from 20 tRNA synthetase genes and their extracellular targets, such as neuropilin-2 (NRP2).

Our primary focus is on ATYR1923, a clinical stage product candidate which binds to the NRP2 receptor and is designed to down regulate immune engagement in interstitial lung diseases (ILDs). ATYR1923, a fusion protein comprised of the immuno-modulatory domain of histidyl tRNA synthetase (HARS) fused to the fragment crystallizable (FC) region of a human antibody, is a selective modulator of NRP2 that downregulates the innate and adaptive immune response in inflammatory disease states. We are developing ATYR1923 as a potential therapeutic for patients with ILDs, a group of immune-mediated disorders that cause progressive fibrosis of the lung tissue. We selected pulmonary sarcoidosis as our first ILD indication and are currently enrolling a proof-of-concept Phase 1b/2a clinical trial in patients. The study has been designed to evaluate the safety, tolerability and immunogenicity of multiple doses of ATYR1923 and to evaluate established clinical endpoints and certain biomarkers to assess preliminary activity of ATYR1923. A blinded interim analysis of safety and tolerability, the primary endpoint of our ongoing Phase 1b/2a clinical trial, showed study drug (ATYR1923 or placebo) was observed to be generally well tolerated with no drug-related serious adverse events (SAEs), consistent with the earlier Phase 1 study results in healthy volunteers. The final results of our current Phase 1b/2a clinical trial will guide future development of ATYR1923 in pulmonary sarcoidosis and provide insight for the potential of ATYR1923 in other ILDs, such as chronic hypersensitivity pneumonitis (CHP) and connective tissue disease ILD (CTD-ILD).

In January 2020, we entered into a license with Kyorin Pharmaceutical Co., Ltd. (Kyorin) for the development and commercialization of ATYR1923 for ILDs in Japan. Under the collaboration and license agreement with Kyorin (the Kyorin Agreement), Kyorin received an exclusive right to develop and commercialize ATYR1923 in Japan for all forms of ILDs. We received an \$8.0 million upfront payment and we are eligible to receive an additional \$167.0 million in the aggregate upon achievement of certain development, regulatory and sales milestones, as well as tiered royalties ranging from the mid-single digits to mid-teens on net sales in Japan. Under the terms of the Kyorin Agreement, Kyorin will fund all research, development, regulatory, marketing and commercialization activities in Japan, as well as support our global development efforts for ATYR1923.

In conjunction with our clinical development of ATYR1923, we have in parallel been expanding our knowledge of NRP2 antibodies and tRNA synthetases.

NRP2 is a receptor that plays a key role in lymphatic development and in regulating inflammatory responses. In many forms of cancer, high NRP2 expression is associated with worse outcomes. NRP2 can interact with multiple ligands and coreceptors to influence their functional roles. We are actively investigating NRP2 receptor biology, both internally and in collaboration with key academic thought leaders, to identify new product candidates for a variety of disease settings, including cancer, inflammation, and lymphangiogenesis. We have generated a panel of certain NRP2 antibodies that we believe have potential therapeutic value in oncology and are currently evaluating such antibodies in experimental models. We are also working closely with other collaborators and academia to further research in these areas. For example, in January 2019, we expanded a successful pilot study and entered into a research collaboration with the University of Nebraska Medical Center (UNMC) and Dr. Kaustubh Datta, who has published extensively in the

field of NRP2 biology. In October 2019, we entered into a research collaboration with Dr. Diane Bielenberg at Boston Children's Hospital, an expert in NRP2 biology, to examine the therapeutic efficacy of anti-NRP2 antibodies in potential new roles and indications. Dr. Bielenberg's research will initially explore conditions characterized by inappropriate smooth muscle contractility, such as urinary incontinence and gastrointestinal tract motility disorders, where current treatments often have limited efficacy and serious side effects.

Our continued research of tRNA synthetases is being conducted through both industry and academic collaborations. In March 2019, we entered into a research collaboration and option agreement with CSL Behring (CSL) for the development of product candidates derived from up to four tRNA synthetases from our preclinical pipeline. Under the terms of the collaboration, CSL is obligated to fund all research and development activities and will pay a total of \$4.25 million per synthetase program (\$17.0 million if all four synthetase programs advance) in option fees based on achievement of research milestones and CSL's determination to continue development.

In May 2018, we implemented a corporate restructuring and program prioritization plan (Restructuring Plan) to streamline our operations and concentrate development efforts on the advancement of our therapeutic candidate, ATYR1923. In connection with the Restructuring Plan, we reduced our workforce by approximately 30% to 42 full-time employees. We completed the workforce reduction in June 2018. We recorded charges of approximately \$0.9 million for employee severance and other related termination benefits and approximately \$0.4 million in one-time, non-cash stock-based compensation charges due to the acceleration of time-based vesting provisions of outstanding equity awards in accordance with our Executive Severance and Change in Control Policy.

## **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 our accounts and our 98% majority-owned subsidiary in Hong Kong, Pangu BioPharma Limited, as of December 31, 2019. All intercompany transactions and balances are eliminated in consolidation.

### ***Leases***

On January 1, 2019, we adopted Accounting Standards Update (ASU) No. 2016-02, *Leases (Topic 842)* (ASU No. 2016-02). For our long-term operating leases, we recognized a right-of-use asset and a lease liability in our consolidated balance sheets. The lease liability is determined as the present value of future lease payments using an estimated rate of interest that we would pay to borrow equivalent funds on a collateralized basis at the lease commencement date. The right-of-use asset is based on the liability adjusted for any prepaid or deferred rent. We determined the lease term at the commencement date by considering whether renewal options and termination options are reasonably assured of exercise.

We elected the package of practical expedients permitted under the transition guidance within the new standard, which among other things, allowed us to exclude from our consolidated balance sheets recognition of leases having a term of 12 months or less (short-term leases) and we elected to not separate lease components and non-lease components for our long-term leases.

Rent expense for the operating lease is recognized on a straight-line basis over the lease term and is included in operating expenses in our consolidated statements of operations.

Prior period amounts continue to be reported in accordance with our historical accounting practices under previous lease guidance, Accounting Standards Codification (ASC) 840, *Leases*. See "—Recent Accounting Pronouncements" in Note 1 to our consolidated financial statements included elsewhere in this Annual Report, for more information about the impact of the adoption on ASU No. 2016-02.

### ***Revenue Recognition***

In March 2019, we entered into a research collaboration and option agreement with CSL for the development of product candidates derived from up to four tRNA synthetases from our preclinical pipeline (CSL Agreement). Under the terms of the CSL Agreement, CSL will fund all research and development activities related to the development of the applicable product candidates for the duration of the collaboration. CSL reimburses us for all research and development activities. The research and development activities will be performed in six phases by both parties. The first phase totaling \$0.6 million was funded in May 2019 and future phases will be funded on a quarterly basis.

In addition, CSL will pay a total of up to \$4.25 million per synthetase program (\$17 million if all four synthetase programs advance) in option fees based on achievement of research milestones and CSL's determination to continue development. As of December 31, 2019, no research milestones had been met. We will grant CSL an option to negotiate licenses for worldwide rights to each investigational new drug (IND) candidate that emerges from this research collaboration. Specific license terms will be negotiated during an exclusivity period following the exercise of each program option.

CSL has the right to terminate the research collaboration and option agreement in its entirety or with respect to one or more synthetases upon 45 days' notice. Either party has the right to terminate the agreement upon material breach of obligation or insolvency of the other party.

For the year ended December 31, 2019, we recognized \$422,000 as collaboration revenue under the CSL Agreement.

### ***Research and Development Expenses***

To date, our research and development expenses have related primarily to the development of, and clinical trials for, our product candidates, and to research efforts targeting the potential therapeutic application of other tRNA synthetase-based immuno-modulators (including funding of our former research collaboration with The Scripps Research Institute) and, more recently research efforts related to NRP2 biology. 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 (CROs) and investigative sites;
- costs for laboratory supplies; and
- allocated facilities, depreciation and other allocable expenses.

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 our ATYR1923 Phase 1b/2a clinical trial and research, and other potential therapeutics based on our tRNA synthetase biology and NRP2 biology.

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. In particular, as a result of the recent COVID-19 outbreak in the United States, many clinical trial sites in our ongoing Phase 1b/2a clinical trial have temporarily suspended dosing of previously-enrolled patients and/or enrollment of new patients. As a result, we anticipate that the availability of top-line results from the clinical trial will be delayed. This delay may also cause certain research and development expenses related to the trial to be incurred in future quarters, and ultimately, the incurrence of such expenses related to the clinical trial could shift materially. 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)***

In November 2016, we entered into a loan and security agreement, as amended (Loan Agreement) with Silicon Valley Bank and Solar Capital Ltd. (Lenders) to borrow up to \$20.0 million issuable in three separate tranches (the 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. Other income (expense), net consists primarily of interest income earned on cash, cash equivalents and investments and interest expense on our Term Loans outstanding with the Lenders as discussed below.

## 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 (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 that our accounting policies related to research and development expense accruals 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 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 our accrual or prepaid expenses 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 have been no material differences between our estimates and the amounts actually incurred.

## Results of Operations

### Comparison of the Years Ended December 31, 2019 and 2018

The following table summarizes our results of operations for the years ended December 31, 2019 and 2018 (in thousands):

	Years Ended December 31,		Increase / (Decrease)
	2019	2018	
Revenues	\$ 422	\$ —	\$ 422
Research and development expenses	14,048	20,385	(6,337)
General and administrative expenses	9,352	12,435	(3,083)
Other income (expense), net	(785)	(1,695)	(910)

*Revenues.* Revenues consist of collaboration revenue under our research collaboration and option agreement with CSL.

*Research and development expenses.* Research and development expenses were \$14.0 million and \$20.4 million for the years ended December 31, 2019 and 2018, respectively. The decrease of \$6.4 million was due primarily to a \$2.8 million decrease in personnel associated costs mainly as a result a reduction in force initiated in May 2018, a decrease of \$1.7 million in costs associated with our research collaboration with The Scripps Research Institute which we terminated effective November 2018, a \$1.7 million decrease in preclinical research and development expenses and a decrease of \$0.7 million related to lower product manufacturing costs. The decrease was partially offset by an increase of \$0.7 million related to our ATYR1923 Phase 1b/2a clinical trial.

*General and administrative expenses.* General and administrative expenses were \$9.4 million and \$12.4 million for the years ended December 31, 2019 and 2018, respectively. The decrease of \$3.0 million was due primarily to a \$2.2 million decrease in personnel associated costs mainly as a result of the May 2018 reduction in force, and a \$0.8 million decrease in professional fees.

*Other income (expense), net.* Other income (expense), net was \$0.8 million and \$1.7 million for the years ended December 31, 2019 and 2018, respectively. The \$0.9 million decrease was primarily a result of lower principal balances on our Term Loans with our Lenders which we started repaying in June 2018.

#### **Comparison of the Years Ended December 31, 2018 and 2017**

The following table summarizes our results of operations for the years ended December 31, 2018 and 2017 (in thousands):

	<b>Years Ended December 31,</b>		<b>Increase / (Decrease)</b>
	<b>2018</b>	<b>2017</b>	
Research and development expenses	\$ 20,385	\$ 30,067	(9,682)
General and administrative expenses	12,435	17,078	(4,643)
Other income (expense), net	(1,695)	(1,062)	633

*Research and development expenses.* Research and development expenses were \$20.4 million and \$30.1 million for the years ended December 31, 2018 and 2017, respectively. The decrease of \$9.7 million was due primarily to a \$4.2 million decrease related to the completion of preclinical and certain clinical studies related to ATYR1923 and ATYR1940, a \$3.3 million decrease in product manufacturing costs, a \$1.7 million decrease in personnel associated costs due to lower headcount, which was mainly a result of the Restructuring Plan, a \$1.4 million decrease in overall general research and development expenses and a \$0.2 million decrease in non-cash stock-based compensation expense. The decrease was partially offset by an increase of \$1.1 million related to the initiation of our ATYR1923 Phase 1b/2a clinical trial.

*General and administrative expenses.* General and administrative expenses were \$12.4 million and \$17.1 million for the years ended December 31, 2018 and 2017, respectively. The decrease of \$4.6 million was due primarily to a \$3.2 million decrease in non-cash stock-based compensation expense due to executive transitions in 2017, a \$0.6 million decrease in personnel associated costs due to lower headcount, which was mainly a result of the Restructuring Plan and a \$0.8 million decrease in intellectual property and legal expenses.

*Other income (expense), net.* Other expense was \$1.7 million and \$1.1 million for the years ended December 31, 2018 and 2017, respectively. The \$0.6 million increase was primarily a result of increased interest expense related to our Term Loans.

#### **Liquidity and Capital Resources**

We have incurred losses and negative cash flows from operations since our inception. As of December 31, 2019, we had an accumulated deficit of \$322.3 million and we expect to continue to incur net losses for the foreseeable future. As of December 31, 2019, we had cash, cash equivalents and available-for-sale investments of \$31.1 million. Since that time, we received \$8.0 million related to the Kyorin Agreement and approximately \$20.7 million in gross proceeds from our underwritten follow-on public offering of common stock, before deducting underwriting discounts, commissions and offering expenses payable by us. We believe that our current cash, cash equivalents and available-for-sale investments, will be sufficient to meet our anticipated cash requirements for a period of at least one year from the date of this Annual Report.

#### **Sources of Liquidity**

From our inception through December 31, 2019, we have financed our operations primarily through the sale of equity securities and convertible debt and through venture debt and term loans.

#### **Debt Financing**

We have a Loan Agreement with our Lenders for the Term Loans. Under the Loan Agreement, we are obligated to make interest-only payments through June 1, 2018, followed by consecutive equal monthly payments of principal and interest in arrears through the

maturity date of November 18, 2020. Accordingly, we started paying the principal balance of the Term Loans in June 2018. 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 Term Loans in full, subject to a prepayment fee ranging from 1.0% to 3.0% depending upon when the prepayment occurs, including any non-usage fees. We intend to retire the outstanding amounts due under our Loan Agreement at the maturity date in November 2020.

In connection with the first tranche, we issued warrants to each of the Lenders to purchase an aggregate of 3,415 shares of our common stock with an exercise price of \$43.93 per share. In connection with the second tranche, we issued warrants to each of the Lenders to purchase an aggregate of 1,489 shares of our common stock with an exercise price of \$50.37 per share. In connection with the third tranche, we issued warrants to each of the Lenders to purchase an aggregate of 1,443 shares of our common stock with an exercise price of \$51.98 per share. The warrants are immediately exercisable and have a maximum contractual term of seven years.

### **Sales of Equity Securities**

In June 2016, we entered into a sales agreement with Cowen and Company, LLC (Cowen) for an at-the-market offerings program (ATM Offering Program), under which we were able to offer and sell shares of our common stock having an aggregate offering price of up to \$35.0 million from time to time. In May 2019, we terminated the ATM Offering Program with Cowen. Under the ATM Offering Program with Cowen, we sold an aggregate of 243,393 shares of common stock at an average price of \$7.88 per common share for net proceeds of \$1.8 million.

In May 2019, we entered into a sales agreement with H.C. Wainwright & Co., LLC (Wainwright) for an ATM Offering Program under which we may offer and sell shares of our common stock having an aggregate offering price of up to \$10.0 million. Wainwright is entitled to a commission at a fixed commission rate equal to 3% of the gross proceeds. Under the ATM Offering Program with Wainwright, as of December 31, 2019, we had sold an aggregate of 611,687 shares of common stock at an average price of \$5.43 per common share for net proceeds of \$3.0 million.

In February 2020, we completed an underwritten follow-on public offering of 4,235,294 shares of our common stock at a price to the public of \$4.25 per share. In March 2020, the underwriters fully exercised their over-allotment option for the issuance of an additional 635,294 shares of common stock. The total gross proceeds from the underwritten follow-on public offering, including the over-allotment, was approximately \$20.7 million, before deducting underwriting discounts, commissions and offering expenses payable by us. We anticipate using the net proceeds from the offering for general corporate purposes, including clinical trial expenses, research and development expenses, manufacturing expenses, and general administrative expenses.

### **Cash Flows**

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

	<b>Years Ended December 31,</b>		
	<b>2019</b>	<b>2018</b>	<b>2017</b>
Net cash (used in) provided by:			
Operating activities	\$ (20,013)	\$ (31,063)	\$ (42,364)
Investing activities	4,925	37,172	(27,637)
Financing activities	1,336	(4,238)	52,704
Net change in cash and cash equivalents	<u>\$ (13,752)</u>	<u>\$ 1,871</u>	<u>\$ (17,297)</u>

*Operating activities.* Net cash used in operating activities was \$20.0 million, \$31.1 million and \$42.4 million for the years ended December 31, 2019, 2018 and 2017, 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, 2019 related to non-cash charges including: \$0.6 million for depreciation, \$1.8 million for stock-based compensation, \$0.7 million for debt discount accretion and non-cash interest expense, \$0.7 million for accretion of a right-of-use asset and a \$0.2 million decrease in our net operating assets and liabilities. The primary differences between net cash used in operating activities and our net loss in the year ended December 31, 2018 related to non-cash charges including: \$0.7 million for depreciation and amortization, \$3.4 million for stock-based compensation, \$1.0 million for debt discount accretion and non-cash interest expense, and a \$1.4 million increase in our net operating assets and liabilities. 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, \$6.8 million for stock-based compensation, \$0.6 million for debt discount accretion and non-cash interest expense and a \$2.1 million increase in our net operating assets and liabilities.

*Investing activities.* Net cash provided by investing activities for the year ended December 31, 2019 consisted of \$5.0 million of net maturities of investment securities. Net cash provided in investing activities for the year ended December 31, 2018 consisted of \$37.8 million of net maturities of investment securities offset in part by \$0.6 million of property and equipment purchases. 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.

*Financing activities.* Net cash provided by financing activities for the year ended December 31, 2019 was \$1.3 million and consisted primarily of \$4.4 million in proceeds from at the market issuances of common stock, net of issuance costs, and \$4.9 million in proceeds from a registered direct offering, net of issuance costs, offset in part by \$8.0 million of principal payments on the Term Loans. Net cash used by financing activities during the year ended December 31, 2018 was \$4.2 million and consisted primarily of \$4.7 million of principal payments on the Term Loans, partially offset by \$0.4 million of net proceeds from the at the market issuances of common stock, net of issuance costs. 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 a private placement of equity securities, net of offering costs paid in the period and \$9.9 million from the second and third tranches of the Term Loans, net of issuance costs.

### **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 ATYR1923 in clinical development, continue our research and development activities with respect to other potential therapies based on tRNA synthetase biology and NPR2 biology, 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. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations. Our forecast of the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement that involves risks and uncertainties, and actual results could vary materially.

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

- our ability to initiate, and the progress and results of, our current and planned clinical trials of ATYR1923;
- delays of our current and planned clinical trials of ATYR 1923 and any resulting cost increases as a result of the COVID-19 outbreak;
- the number and characteristics of product candidates that we pursue;
- the scope, progress, results and costs of preclinical development, and clinical trials for other product candidates;
- the manufacturing of preclinical study and clinical trial materials;
- our ability to maintain existing and enter into new collaboration and licensing arrangements and the timing of any payments we may receive under such arrangements;
- 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, grant funding, collaborations, strategic partnerships and/or licensing arrangements, and when we are closer to commercialization of our product candidates potentially through debt financings. To the extent we raise additional capital through the sale of equity, 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. 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. The incurrence of additional indebtedness would increase our fixed payment obligations and may require us to agree to certain restrictive covenants, such as limitations on our ability to incur additional debt, limitations on our ability to acquire, sell or license intellectual property rights and other operating restrictions that could adversely impact our ability to conduct our business. We may be unable to raise additional funds on acceptable terms or at all. The impact of COVID-19 on capital markets may affect the availability, amount and type of financing available to us in the future. If we are unable to raise additional funds, 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, 2019:

	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 including final payment	\$ 9,083	\$ 9,083	\$ —	\$ —	\$ —
Facilities lease (1)	2,994	754	1,842	398	—
<b>Total</b>	<b>\$ 12,077</b>	<b>\$ 9,837</b>	<b>\$ 1,842</b>	<b>\$ 398</b>	<b>\$ —</b>

- (1) Our operating lease obligations relate to our corporate headquarters in San Diego, California. We have 20,508 square feet of office and laboratory space under an operating lease that expires in May 2023.

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.

### Recent Accounting Pronouncements

For discussion of recently issued accounting pronouncements, refer to the Section titled “Recent Accounting Pronouncements” within Note 2 of our consolidated 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, 2019, we had cash, cash equivalents, and available-for-sale investments totaling \$31.1 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 securities, high quality marketable debt instruments of corporations and financial institutions, and government sponsored and asset-backed securities with contractual maturity dates of less than one year. If interest rates were to increase instantaneously and uniformly by 100 basis points, compared to interest rates as of December 31, 2019, the increase would not have had a material effect on our results of operations.

We do not believe that our cash, cash equivalents and available-for-sale 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 Loans. A one percentage point increase in interest rates would increase expense by approximately \$0.1 million annually and would not materially affect our results of operations.



**Foreign Currency Exchange Risk**

We incur expenses, including for 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, Hong Kong dollar 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 on 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.

**Report of Independent Registered Public Accounting Firm**

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

**Opinion on the Financial Statements**

We have audited the accompanying consolidated balance sheets of aTyr Pharma, Inc. (the Company) as of December 31, 2019 and 2018, the related consolidated statements of operations, comprehensive loss, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2019, 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, 2019 and 2018, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2019, in conformity with U.S. generally accepted accounting principles.

**Adoption of ASU No. 2016-02**

As discussed in Note 2 to the consolidated financial statements, the Company changed its method of accounting for leases in 2019 due to the adoption of Accounting Standards Update (ASU) No. 2016-02, Leases (Topic 842), and the related amendments

**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 26, 2020

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

	<b>December 31,</b>	
	<u>2019</u>	<u>2018</u>
<b>Assets</b>		
Current assets:		
Cash and cash equivalents	\$ 9,210	\$ 22,962
Available-for-sale investments, short-term	21,934	26,583
Prepaid expenses and other assets	781	1,258
Total current assets	<u>31,925</u>	<u>50,803</u>
Property and equipment, net	1,270	1,853
Right-of-use assets	2,821	—
Other assets	172	90
Total assets	<u>\$ 36,188</u>	<u>\$ 52,746</u>
<b>Liabilities and Stockholders' Equity</b>		
Current liabilities:		
Accounts payable	\$ 847	\$ 1,040
Accrued expenses	2,376	2,026
Contract liability	208	—
Current portion of operating lease liability	755	—
Current portion of long-term debt, net of issuance costs and discount	8,737	7,767
Total current liabilities	<u>12,923</u>	<u>10,833</u>
Long-term operating lease liability, net of current portion	2,239	—
Long-term debt, net of current portion and issuance costs and discount	—	8,263
Commitments and contingencies (Note 6)		
Stockholders' equity:		
Preferred stock, \$0.001 par value per share; 5,000,000 undesignated authorized shares; Class X Convertible Preferred Stock issued and outstanding shares – 1,643,961 and 2,285,952 as of December 31, 2019 and 2018, respectively	2	2
Common stock, \$0.001 par value per share; 10,714,286 authorized shares; issued and outstanding shares – 3,891,787 and 2,186,389 as of December 31, 2019 and 2018, respectively	4	2
Additional paid-in capital	343,524	332,407
Accumulated other comprehensive loss	(40)	(60)
Accumulated deficit	(322,304)	(298,701)
Total aTyr Pharma stockholders' equity	<u>21,186</u>	<u>33,650</u>
Noncontrolling interest in Pangu BioPharma Limited	(160)	—
Total stockholders' equity	<u>21,026</u>	<u>33,650</u>
Total liabilities and stockholders' equity	<u>\$ 36,188</u>	<u>\$ 52,746</u>

*See accompanying notes.*

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

	<b>Years Ended December 31,</b>		
	<b>2019</b>	<b>2018</b>	<b>2017</b>
<b>Revenues:</b>			
Collaboration revenue	\$ 422	\$ —	\$ —
Total revenues	422	—	—
<b>Operating expenses:</b>			
Research and development	\$ 14,048	\$ 20,385	\$ 30,067
General and administrative	9,352	12,435	17,078
Total operating expenses	23,400	32,820	47,145
Loss from operations	(22,978)	(32,820)	(47,145)
Total other expense, net	(785)	(1,695)	(1,062)
Consolidated net loss	(23,763)	(34,515)	(48,207)
Net loss attributable to noncontrolling interest in Pangu BioPharma Limited	160	—	—
Net loss attributable to aTyr Pharma, Inc.	(23,603)	(34,515)	(48,207)
Net loss per share attributable to common stockholders, basic and diluted	\$ (7.03)	\$ (16.11)	\$ (26.13)
Weighted average common stock shares outstanding, basic and diluted	3,355,600	2,141,961	1,845,033

*See accompanying notes.*

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

	Years Ended December 31,		
	2019	2018	2017
Consolidated net loss	\$ (23,763)	\$ (34,515)	\$ (48,207)
Other comprehensive gain (loss):			
Change in unrealized gain (loss) on available-for-sale investments, net of tax	20	60	(44)
Comprehensive loss	(23,743)	(34,455)	(48,251)
Comprehensive loss attributable to noncontrolling interest Pangu BioPharma Limited	160	—	—
Comprehensive loss attributable to aTyr Pharma, Inc. common stockholders	\$ (23,583)	\$ (34,455)	\$ (48,251)

*See accompanying notes.*

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

	<u>Convertible Preferred Stock</u>		<u>Common Stock</u>		<u>Additional Paid-In Capital</u>	<u>Other Comprehensive Gain/(Loss)</u>	<u>Accumulated Deficit</u>	<u>Noncontrolling Interest</u>	<u>Total Stockholders' Equity</u>
	<u>Shares</u>	<u>Amount</u>	<u>Shares</u>	<u>Amount</u>					
Balance as of December 31, 2016	—	\$ —	1,698,252	\$ 2	\$ 278,854	\$ (76)	\$ (215,979)	\$ —	\$ 62,801
Exercise of common stock options and release of restricted stock units	—	—	7,914	—	186	—	—	—	186
Issuance of common stock pursuant to employee stock purchase plan	—	—	4,364	—	175	—	—	—	175
Issuance of common stock and preferred stock from private placement, net of offering costs	2,285,952	2	419,438	—	42,237	—	—	—	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, net of tax	—	—	—	—	—	(44)	—	—	(44)
Net loss	—	—	—	—	—	—	(48,207)	—	(48,207)
Balance as of December 31, 2017	2,285,952	2	2,129,968	2	328,547	(120)	(264,186)	—	64,245
Exercise of common stock options and release of restricted stock units	—	—	3,670	—	14	—	—	—	14
Issuance of common stock pursuant to employee stock purchase plan	—	—	3,028	—	36	—	—	—	36
Issuance of common stock from at the market offerings, net of offering costs	—	—	49,723	—	379	—	—	—	379
Stock-based compensation	—	—	—	—	3,431	—	—	—	3,431
Net unrealized gain on investments, net of tax	—	—	—	—	—	60	—	—	60
Net loss	—	—	—	—	—	—	(34,515)	—	(34,515)
Balance as of December 31, 2018	2,285,952	2	2,186,389	2	332,407	(60)	(298,701)	—	33,650
Conversion of preferred stock to common stock	(641,991)	—	229,283	—	—	—	—	—	—
Issuance of common stock upon release of restricted stock units	—	—	7,487	—	—	—	—	—	—
Issuance of common stock pursuant to employee stock purchase plan	—	—	3,117	—	13	—	—	—	13
Issuance of common stock from at the market offerings, net of offering costs	—	—	805,357	1	4,404	—	—	—	4,405
Issuance of common stock from registered direct offering, net of offering costs	—	—	660,154	1	4,917	—	—	—	4,918
Stock-based compensation	—	—	—	—	1,783	—	—	—	1,783
Net unrealized gain on investments, net of tax	—	—	—	—	—	20	—	—	20
Net loss	—	—	—	—	—	—	(23,603)	(160)	(23,763)
Balance as of December 31, 2019	1,643,961	\$ 2	3,891,787	\$ 4	\$ 343,524	\$ (40)	\$ (322,304)	\$ (160)	\$ 21,026

See accompanying notes.

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

	<b>Years Ended December 31,</b>		
	<b>2019</b>	<b>2018</b>	<b>2017</b>
<b>Cash flows from operating activities:</b>			
Consolidated net loss	\$ (23,763)	\$ (34,515)	\$ (48,207)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	635	746	713
Stock-based compensation	1,783	3,431	6,784
Debt discount accretion and non-cash interest expense	707	966	590
Amortization (accretion) of premium (discount) of available-for-sale investment securities	(284)	(261)	14
Amortization of right-of-use assets	731	—	—
(Gain) loss on disposal of property and equipment	(28)	18	—
Deferred rent	—	—	(130)
Changes in operating assets and liabilities			
Prepaid expenses and other assets	334	610	761
Accounts payable and accrued expenses	162	(2,058)	(2,889)
Contract liability	208	—	—
Operating lease liability	(498)	—	—
Net cash used in operating activities	<u>(20,013)</u>	<u>(31,063)</u>	<u>(42,364)</u>
<b>Cash flows from investing activities:</b>			
Purchases of property and equipment	(79)	(594)	(1,312)
Purchases of available-for-sale investment securities	(40,647)	(40,299)	(77,672)
Maturities of available-for-sale investment securities	45,600	78,065	51,347
Proceeds from sale of property and equipment	51	—	—
Net cash provided by (used in) investing activities	<u>4,925</u>	<u>37,172</u>	<u>(27,637)</u>
<b>Cash flows from financing activities:</b>			
Proceeds from issuance of common stock through employee stock purchase plan	13	36	175
Proceeds from issuance of common stock through option exercises and release of restricted stock units	—	14	186
Proceeds from issuance of common stock through at the market offerings, net of offering costs	4,405	379	—
Proceeds from issuance of common stock through registered direct offering, net of offering costs	4,918	—	—
Proceeds from issuance of securities in the Private Placement, net of issuance costs	—	—	42,477
Proceeds from borrowing, net	—	—	9,866
Repayments on borrowings	(8,000)	(4,667)	—
Net cash provided by (used in) financing activities	<u>1,336</u>	<u>(4,238)</u>	<u>52,704</u>
Net change in cash and cash equivalents	<u>(13,752)</u>	<u>1,871</u>	<u>(17,297)</u>
Cash and cash equivalents at beginning of period	22,962	21,091	38,388
Cash and cash equivalents at the end of period	<u>\$ 9,210</u>	<u>\$ 22,962</u>	<u>\$ 21,091</u>
<b>Supplemental disclosure of cash flow information:</b>			
Interest paid	<u>\$ 1,122</u>	<u>\$ 1,700</u>	<u>\$ 1,000</u>
Purchase of fixed assets included in accounts payable	<u>\$ —</u>	<u>\$ 4</u>	<u>\$ 260</u>
<b>Supplemental schedule of noncash investing and financing activities:</b>			
Issuance of warrants in connection with borrowings	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 263</u>
Changes in share repurchase liability	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 48</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 development of innovative medicines based on novel immunological pathways.

**Principles of Consolidation**

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

**Reverse Stock Split**

In June 2019, we filed a Certificate of Amendment to our Restated Certificate of Incorporation with the Secretary of State of the State of Delaware to effect a 1-for-14 reverse stock split of our issued and outstanding common stock. The reverse stock split became effective at 5:00 p.m. Eastern Time on June 28, 2019 and our common stock began trading on a split-adjusted basis on The Nasdaq Capital Market on July 1, 2019. Our consolidated financial statements and these notes give retrospective effect to the reverse stock split for all periods presented. All issued and outstanding common stock, options and warrants exercisable for common stock, restricted stock units, preferred stock conversions to common stock and per share amounts contained in our consolidated financial statements have been retrospectively adjusted.

**Liquidity and Financial Condition**

We have incurred losses and negative cash flows from operations since our inception. As of December 31, 2019, we had an accumulated deficit of \$322.3 million and we expect to continue to incur net losses for the foreseeable future. As of December 31, 2019, our cash, cash equivalents and available-for-sale investments were \$31.1 million. Since that time, we received \$8.0 million related to the Kyorin Agreement and approximately \$20.7 million in gross proceeds from our underwritten follow-on public offering of common stock, before deducting underwriting discounts, commissions and offering expenses payable by us. We believe that our current cash, cash equivalents and available-for-sale investments, will be sufficient to meet our anticipated cash requirements for a period of at least one year from the date of this Annual Report.

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 to fund our operations. 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 equity offerings, grant funding, collaborations, strategic partnerships and/or licensing arrangements, and when we are closer to commercialization of our product candidates potentially through debt financings. However, we may be unable to raise additional capital or enter into such arrangements when needed on favorable terms or at all. Our failure to raise capital or enter into such arrangements when needed would have a negative impact on our financial condition and ability to develop our product candidates.

In May 2018, we implemented a corporate restructuring and program prioritization plan (Restructuring Plan) to streamline our operations and concentrate development efforts on the advancement of our therapeutic candidate, ATYR1923. In connection with the Restructuring Plan, we reduced our workforce by approximately 30% to 42 full-time employees. We completed the workforce reduction in June 2018. We recorded charges of approximately \$0.9 million for employee severance and other related termination benefits and approximately \$0.4 million in one-time, non-cash stock-based compensation charges due to the acceleration of time-based vesting provisions of outstanding equity awards in accordance with our Executive Severance and Change in Control Policy.



## **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 liabilities in our consolidated financial statements and accompanying notes. The most significant estimates in our consolidated financial statements relate to the fair value of equity issuances and awards, and clinical trial and research and development expenses. Although these estimates are based on our knowledge of current events and actions we may undertake in the future, actual results may ultimately differ materially from these estimates and assumptions.

## **Segment Reporting**

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

## **Reclassifications**

Certain reclassifications have been made to prior year amounts to conform to the current year presentation. The reclassifications were not material to the consolidated financial statements.

## **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 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, 2019, we held an aggregate total of \$21.9 million of investment securities which consisted of corporate debt securities, asset-backed securities, and commercial paper all of which will mature in less than one year, and there was an unrealized gain of \$8,500 between the amortized cost and fair value of these investment securities. As of December 31, 2018, we held \$26.6 million of corporate debt securities, asset-backed securities and United States Treasury securities, all of which mature in less than one year, and there was an unrealized loss of \$10,000 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

Expenses related to clinical studies, preclinical development activities and product manufacturing are based on estimates of the services received and efforts expended pursuant to our contract arrangements. There may be instances in which payments made to our service providers will temporarily exceed the level of services provided and result in a prepayment of the expense. Payments under some of these contracts depend on factors such as, for clinical studies, the successful enrollment of patients, site initiation and the completion of clinical milestones. We make estimates of our accrued expenses as of each balance sheet date based on facts and circumstances known at the time. 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 expense balance accordingly. Historically, our estimated accrued liabilities have materially approximated actual expenses incurred.

## Leases

In January 2019, we adopted Accounting Standards Update (ASU) No. 2016-02, *Leases (Topic 842)* (ASU No. 2016-02). For our long-term operating leases, we recognized a right-of-use asset and a lease liability in our consolidated balance sheets. The lease liability is determined as the present value of future lease payments using an estimated rate of interest that we would pay to borrow equivalent funds on a collateralized basis at the lease commencement date. The right-of-use asset is based on the liability adjusted for any prepaid or deferred rent. We determine the lease term at the commencement date by considering whether renewal options and termination options are reasonably assured of exercise.

We elected the package of practical expedients permitted under the transition guidance within the new standard, which among other things, allowed us to exclude from our consolidated balance sheets recognition of leases having a term of 12 months or less (short-term leases) and we elected to not separate lease components and non-lease components for our long-term leases.

Rent expense for the operating lease is recognized on a straight-line basis over the lease term and is included in operating expenses in our consolidated statements of operations.

Prior period amounts continue to be reported in accordance with our historical accounting practices under previous lease guidance, Accounting Standards Codification (ASC) 840, *Leases*. See “—Recent Accounting Pronouncements” below, for more information about the impact of the adoption on ASU No. 2016-02.

## Revenue Recognition

We have entered into a research collaboration and option agreement with CSL Behring (CSL). The terms of this arrangement include payments to us for research and development services and potential development milestone payments. Performance of obligations under the agreement began in the second quarter of 2019.

We evaluate our agreements under ASC 606, *Revenue from Contracts with Customers (Topic 606)* and ASC 808, *Collaborative Arrangements (Topic 808)*. We recognize revenue when we transfer promised goods or services to customers in an amount that reflects the consideration to which we expect to be entitled in exchange for those goods or services. In determining the appropriate amount of revenue to be recognized as we fulfill our obligations under our agreement, we perform the following steps: (i) identification of the promised goods or services in the contract; (ii) determination of whether the promised goods or services are performance obligations including whether they are distinct in the context of the contract; (iii) measurement of the transaction price, including the constraint on variable consideration; (iv) allocation of the transaction price to the performance obligations; and (v) recognition of revenue when (or as) we satisfy each performance obligation. As part of the accounting for these arrangements, we must develop assumptions that require judgment to determine the stand-alone selling price for each performance obligation identified in the contract. We use key assumptions to determine the stand-alone selling price, which may include forecasted revenues, development timelines, reimbursement rates for personnel costs, discount rates and probabilities of technical and regulatory success.

## 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 advisors; costs to acquire, develop and manufacture preclinical study and clinical trial materials; costs incurred under clinical trial agreements with CROs 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 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. We estimate fair value of stock option grants using the Black-Scholes option pricing model. We 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* as guidance for accounting modification.

## 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.

## 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. 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):

	Years Ended December 31,		
	2019	2018	2017
Class X Preferred Stock (if-converted to common stock)	587,445	816,851	816,851
Common stock warrants	13,904	477,639	477,639
Common stock options and restricted stock units	363,553	371,823	333,154
Employee stock purchase plan	1,958	1,610	2,220
	<u>966,860</u>	<u>1,667,923</u>	<u>1,629,864</u>

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

	Years Ended December 31,		
	2019	2018	2017
<b>Numerator:</b>			
Net loss attributable to aTyr Pharma, Inc.	\$ (23,603)	\$ (34,515)	\$ (48,207)
<b>Denominator:</b>			
Weighted average common shares outstanding	3,355,600	2,141,961	1,845,294
Weighted average common shares subject to repurchase	—	—	(261)
Weighted average common shares outstanding - basic and diluted	<u>3,355,600</u>	<u>2,141,961</u>	<u>1,845,033</u>
<b>Net loss per share - basic and diluted</b>	<u>\$ (7.03)</u>	<u>\$ (16.11)</u>	<u>\$ (26.13)</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 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. We adopted ASU No. 2016-02 on January 1, 2019 using the modified retrospective approach and recognized a \$3.5 million right-of-use asset and \$3.5 million lease liability in our consolidated balance sheet for the discounted value of future lease payments from the adoption of this ASU. The adoption did not have any impact on our accumulated deficit.

In June 2016, the FASB issued ASU No. 2016-13, *Financial Instruments – Credit Losses (Topic 326)*, to provide financial statement users with more decision-useful information about the expected credit losses on financial instruments and other commitments to extend credit held by a reporting entity at each reporting date. To achieve this objective, the amendments in ASU No. 2016-13 replace the incurred loss impairment methodology in current GAAP with a methodology that reflects expected credit losses and requires consideration of a broader range of reasonable and supportable information to inform credit loss estimates. ASU No. 2016-13 is effective for fiscal years beginning after December 15, 2020, including periods within those fiscal years. We are currently evaluating the impact of ASU No. 2016-13 and do not expect the adoption of this guidance will have a material impact on our consolidated financial position or results of operations.

In June 2018, the FASB issued ASU No. 2018-07, *Compensation – Stock Compensation (Topic 718)* to expand the scope of Topic 718 to include share-based payment transactions for acquiring goods and services from nonemployees. The amendments in this update require an entity to apply the requirements of Topic 718 to nonemployee awards except for specific guidance on inputs to an option pricing model and the attribution of cost (that is, the period of time over which share-based payment awards vest and the pattern of cost

recognition over that period). The amendments specify that Topic 718 applies to all share-based payment transactions in which a grantor acquires goods or services to be used or consumed in a grantor's own operations by issuing share-based payment awards. The amendments also clarify that Topic 718 does not apply to share-based payments used to effectively provide (1) financing to the issuer or (2) awards granted in conjunction with selling goods or services to customers as part of a contract accounted for under Topic 606, *Revenue from Contracts with Customers*. ASU No. 2018-07 was effective for fiscal years beginning after December 15, 2018 and we adopted it on January 1, 2019. The adoption did not have a material impact on our consolidated financial position or results of operations.

In July 2018, the FASB issued ASU No. 2018-09, *Codification Improvements* to provide updates for technical corrections, clarifications, and other minor improvements that affect a wide variety of Topics in the Codification including *Amendments to Subtopic 718-40, Compensation—Stock Compensation—Income Taxes*, which clarifies that an entity should recognize excess tax benefits (that is, the difference in tax benefits between the deduction for tax purposes and the compensation cost recognized for financial statement reporting) in the period in which the amount of the deduction is determined, including deductions that are taken on the entity's tax return in a different period from when the event that gives rise to the tax deduction occurs and the uncertainty about whether (1) the entity will receive a tax deduction and (2) the amount of the tax deduction is resolved. ASU No. 2018-09 included other Topics which currently do not apply to us. The transition and effective date of ASU No. 2018-09 are based on the facts and circumstances of each amendment. Some of the amendments in ASU No. 2018-09 do not require transition guidance and are effective immediately and others have transition guidance with effective dates for annual periods beginning after December 15, 2018 which we adopted on January 1, 2019. The adoption did not have a material impact on our consolidated financial position or results of operations.

In November 2018, the FASB issued ASU No. 2018-18, *Collaborative Arrangements (Topic 808)* to clarify the interaction between Topic 808 and Topic 606. A collaborative arrangement, as defined by the guidance in Topic 808, is a contractual arrangement under which two or more parties actively participate in a joint operating activity and are exposed to significant risks and rewards that depend on the activity's commercial success. Topic 808 does not provide comprehensive recognition or measurement guidance for collaborative arrangements, and the accounting for those arrangements is often based on an analogy to other accounting literature or an accounting policy election. Some entities apply revenue guidance directly or by analogy to all or part of their arrangements, and others apply a different accounting method as an accounting policy. Those accounting differences result in diversity in practice on how entities account for transactions on the basis of their view of the economics of the collaborative arrangement. We early adopted ASU No. 2018-18 in the second quarter of 2019 and the adoption of this guidance did not have a material impact on our consolidated financial position or results of operations.

In December 2019, the FASB issued ASU No. 2019-12, *Income Taxes (Topic 740), Simplifying the Accounting for Income Taxes* to identify, evaluate, and improve areas of GAAP for which costs and complexity can be reduced while maintaining or improving the usefulness of the information provided to users of financial statements. The amendments for ASU No. 2019-12 simplify the accounting for income taxes by removing certain exceptions to the general principles in Topic 740. The amendments also improve consistent application of and simplify GAAP for other areas of Topic 740 by clarifying and amending existing guidance. ASU No. 2019-12 is effective for fiscal year years beginning after December 15, 2020, and interim periods within those fiscal years. Early adoption is permitted. An entity that elects early adoption must adopt all the amendments in the same period. We are currently evaluating the impact of ASU No. 2019-12 and do not expect the adoption of this guidance 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):

	Total	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)
<b>As of December 31, 2019</b>				
Assets:				
Current:				
Cash equivalents	\$ 8,248	\$ 8,248	\$ —	\$ —
Available-for-sale investments, short-term:				
Asset-backed securities	6,304	—	6,304	—
Commercial paper	7,568	—	7,568	—
Corporate debt securities	8,062	—	8,062	—
Total short-term investments	21,934	—	21,934	—
Total assets measured at fair value	\$ 30,182	\$ 8,248	\$ 21,934	\$ —

	Total	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)
<b>As of December 31, 2018</b>				
Assets:				
Current:				
Cash equivalents	\$ 16,019	\$ 16,019	\$ —	\$ —
Available-for-sale investments, short-term:				
Asset-backed securities	7,773	—	7,773	—
Commercial paper	6,144	—	6,144	—
Corporate debt securities	12,666	—	12,666	—
Total short-term investments	26,583	—	26,583	—
Total assets measured at fair value	\$ 42,602	\$ 16,019	\$ 26,583	\$ —

As of December 31, 2019 and 2018, available-for-sale investments are detailed as follows (in thousands):

	December 31, 2019			
	Gross Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Market Value
Available-for-sale investments, short-term:				
Asset-backed securities	\$ 6,299	\$ 5	\$ —	\$ 6,304
Commercial paper	7,568	—	—	7,568
Corporate debt securities	8,057	5	—	8,062
	\$ 21,924	\$ 10	\$ —	\$ 21,934

	December 31, 2018			
	Gross Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Market Value
Available-for-sale investments, short-term:				
Asset-backed securities	\$ 7,777	\$ —	\$ (4)	\$ 7,773
Commercial paper	6,144	—	—	6,144
Corporate debt securities	12,672	—	(6)	12,666
	<u>\$ 26,593</u>	<u>\$ —</u>	<u>\$ (10)</u>	<u>\$ 26,583</u>

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.

As of December 31, 2019, all available-for-sale investments were in a gross unrealized gain position, and had been in such position for less than twelve months.

#### 4. License Agreement

In March 2019, we entered into a research collaboration and option agreement with CSL for the development of product candidates derived from up to four tRNA synthetases from our preclinical pipeline (CSL Agreement). Under the terms of the CSL Agreement, CSL will fund all research and development activities related to the development of the applicable product candidates for the duration of the collaboration. CSL reimburses us for all research and development activities. The research and development activities will be performed in six phases by both parties. The first phase totaling \$0.6 million was funded in May 2019 and future phases will be funded on a quarterly basis.

In addition, CSL will pay a total of up to \$4.25 million per synthetase program (\$17 million if all four synthetase programs advance) in option fees based on achievement of research milestones and CSL's determination to continue development. As of December 31, 2019, no research milestones had been met. We will grant CSL an option to negotiate licenses for worldwide rights to each investigational new drug (IND) candidate that emerges from this research collaboration. Specific license terms will be negotiated during an exclusivity period following the exercise of each program option.

CSL has the right to terminate the research collaboration and option agreement in its entirety or with respect to one or more synthetases upon 45 days notice. Either party has the right to terminate the agreement upon material breach of obligation or insolvency of the other party.

We assessed our research collaboration with CSL in accordance with Topic 606 and concluded that CSL is a customer. We identified the following performance obligations under the CSL Agreement: 1) research services; and 2) participation in the Joint Steering Committee. We concluded that the performance obligations are interrelated and do not have a standalone basis. CSL has the right to terminate the research collaboration upon 45 days notice, which is considered to be the legally enforceable contract term. Therefore, during the first phase of research services, we have a 45 day performance obligation and all research services beyond the initial 45 days performance obligation are considered a material right. In addition, each phase of research services represents a separate customer option since CSL must provide written notice of its intent to advance to the next phase.

Under the CSL Agreement, CSL is obligated to pay us for the costs incurred by us under the research programs. The payment of \$0.6 million for the first phase of the research program received in May 2019 was considered fixed consideration and we will recognize revenue on the payment for the research service performance obligation as the services are performed. We are utilizing a cost-based input method to measure proportional performance and to calculate the corresponding amount of revenue to recognize. We believe this is the best measure of progress because other measures do not reflect how we transfer the performance obligation to our counterparty. In applying the cost-based input methods of revenue recognition, we use actual costs incurred relative to budgeted costs to fulfill the combined performance obligation. These costs consist primarily of third-party contract costs and internal full-time equivalent effort. A cost-based input method of revenue recognition requires us to make estimates of costs to complete the performance obligations. The cumulative effect of revisions to estimated costs to complete the performance obligations will be recorded in the period in which changes are identified and amounts can be reasonably estimated. A significant change in these assumptions and estimates could have a material impact on the timing and amount of revenue recognized in future periods.

The option fees based on research milestones under the CSL Agreement are variable consideration. Because they are binary in nature, we will use the "most-likely" method to evaluate whether the milestones should be included. However, the milestones are only

payable upon CSL's decision to proceed to the next research phase for any program, and are therefore subject to CSL's sole discretion. Accordingly, the milestones are fully constrained and we will not recognize revenue related to these amounts until we have received notification from CSL that they would like to proceed with the next phase of a research program. For the year ended December 31, 2019, we recognized \$422,000 as collaboration revenue under the CSL Agreement.

## 5. Balance Sheet Details

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

	<b>December 31,</b>	
	<b>2019</b>	<b>2018</b>
Computer and office equipment	\$ 543	\$ 543
Scientific and laboratory equipment	5,241	5,631
Tenant improvements	1,700	1,703
	<u>7,484</u>	<u>7,877</u>
Less accumulated depreciation and amortization	(6,214)	(6,024)
	<u>\$ 1,270</u>	<u>\$ 1,853</u>

As of December 31, 2019, 2018 and 2017, depreciation expense was \$0.6 million, \$0.7 million and \$0.7 million, respectively.

Accrued expenses consist of the following (in thousands):

	<b>December 31,</b>	
	<b>2019</b>	<b>2018</b>
Accrued salaries, wages and benefits	\$ 1,275	\$ 1,309
Other accrued expenses (1)	1,101	717
	<u>\$ 2,376</u>	<u>\$ 2,026</u>

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

## 6. Debt, Commitments and Contingencies

### Term Loans

In November 2016, we entered into a loan and security agreement and subsequently entered amendments (collectively, the Loan Agreement), for term loans with Silicon Valley Bank (SVB) and Solar Capital Ltd. (Solar), to borrow up to \$20.0 million issuable in three separate tranches (the 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.

Under the Loan Agreement, we are obligated to make interest only payments through June 1, 2018, followed by consecutive equal monthly payments of principal and interest in arrears through the maturity date of November 18, 2020. Accordingly, we started paying the Term Loans in June 2018. 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, if invoked, would enable 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, 2019 the carrying value of our Term Loans consisted of \$7.3 million principal outstanding, less the debt issuance costs of \$0.1 million and the accretion of the final maturity payment of \$1.8 million. We intend to pay our Term Loans in full, including the final maturity payment by the fourth quarter of 2020. The debt issuance costs have been recorded as a debt discount, and are being accreted to interest expense over the life of the Term Loans.



In connection with the first tranche, we issued warrants to each of SVB and Solar to purchase an aggregate of 3,415 shares of our common stock with an exercise price of \$43.93 per share. In connection with the second tranche, we issued warrants to each of SVB and Solar to purchase an aggregate of 1,489 shares of our common stock with an exercise price of \$50.37 per share. In connection with the third tranche, we issued warrants to each of SVB and Solar to purchase an aggregate of 1,443 shares of our common stock with an exercise price of \$51.98 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.

## Facility Lease

We adopted ASU No. 2016-02, utilizing the modified retrospective transition method at the beginning of the first quarter of 2019. We elected the package of practical expedients requiring no reassessment of whether any expired or existing contracts are or contain leases, the lease classification of any expired or existing leases, or initial direct costs for any existing leases. We did not elect the hindsight practical expedient. We also made accounting policy elections not to apply the recognition requirements under ASU No. 2016-02 to any of our short-term leases and to account for each separate lease and associated non-lease components as a single lease component for all of our leases. Under ASU No. 2016-02, we determine if an arrangement is a lease at inception. The adoption of the new lease standard had a material impact on the consolidated balance sheets, but did not have a material impact on the consolidated statements of operations. The impact on the consolidated balance sheet resulted in the recording of a \$3.5 million right-of-use asset and a corresponding operating lease liability for the same amount. Our right-of-use assets consist of an operating lease for our facility headquarters. We utilize a discount rate (incremental borrowing rate) of 9.6%. We have 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.

Rent expense for the years ended December 31, 2019, 2018 and 2017 was \$1.0 million, \$1.0 million and \$0.9 million, respectively. As of December 31, 2019, the weighted average remaining lease term was 3.4 years and the weighted average discount rate was 9.6%.

Future minimum payments under the non-cancelable facility lease and reconciliation to the operating lease liability as of December 31, 2019 were as follows (in thousands):

	<b>Operating Lease</b>
2020	\$ 1,002
2021	1,031
2022	1,062
2023	404
Less: Amount representing interest	(505)
Present value of lease payments	2,994
Less: Current portion of operating lease liability	(755)
Long-term operating lease liability	<u>\$ 2,239</u>

## Related Party Transactions

### Research Agreements and Funding Obligations

We provided funding to The Scripps Research Institute (TSRI) pursuant to a research funding and option agreement to conduct certain research activities. We terminated our research funding and option agreement effective as of November 2018. During the years ended December 31, 2018 and 2017, we recognized expense under the agreement in the amount of \$1.7 million and \$1.8 million, respectively. Paul Schimmel, Ph.D., a member of our board of directors, is a faculty member at TSRI and such payments fund a portion of his research activities conducted at TSRI.

## 7. Stockholders' Equity

### Common Stock

#### At the Market Offering Program

In June 2016, we entered into a sales agreement with Cowen and Company, LLC (Cowen) for at the market offerings (ATM Offering Program), under which we were able to offer and sell shares of our common stock having an aggregate offering price of up to \$35.0 million from time to time. In May 2019, we terminated the ATM Offering Program with Cowen. During the year and prior to termination in May 2019, we sold an aggregate of 193,670 shares of common stock at an average price of \$7.35 per common share for net proceeds of \$1.4 million under the ATM Offering Program with Cowen.

In May 2019, we entered into a sales agreement with H.C. Wainwright & Co., LLC (Wainwright) to create an ATM Offering Program under which we may offer and sell shares of our common stock having an aggregate offering price of up to \$10.0 million. Wainwright is entitled to a commission at a fixed commission rate equal to 3% of the gross proceeds. During the year ended December 31, 2019, we sold an aggregate of 611,687 shares of common stock at an average price of \$5.43 per common share for net proceeds of \$3.0 million under the ATM Offering Program with Wainwright.

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

In August 2017, we completed a private placement of common and preferred stock in which 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), purchased preferred stock and common stock. We issued to VGO Fund 126,985 shares of our common stock, at a price of \$37.10 per share, 2,285,952 shares of our Class X Convertible Preferred Stock, par value of \$0.001 at a price of \$13.25 per share, and warrants to purchase up to that number of additional shares of common stock. The remaining Purchasers purchased an aggregate of 292,453 shares of our common stock, at a price of \$37.10 per share, and warrants to purchase up to 109,743 additional shares of our common stock. Gross proceeds from the private placement were \$45.8 million. The warrants to purchase 463,735 shares of our common stock are exercisable at an exercise price of \$64.92 per share, subject to adjustments as provided under the terms of the warrants. The warrants expired on December 31, 2019.

Each share of preferred stock is convertible into approximately 0.357 shares of our common stock. In January 2019, the VGO Fund converted 641,991 shares of its preferred stock into 229,283 shares of common stock.

### **Registered Direct Offering**

In April 2019, we entered into a securities purchase agreement with an institutional investor, The Federated Kaufmann Small Cap Fund, and Paul Schimmel, Ph.D., a member of our board of directors, relating to the issuance and sale of 660,154 shares of our common stock. The shares of common stock were sold in a registered direct offering at a purchase price of \$7.57 per share for gross proceeds of approximately \$5.0 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 112,399 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 automatically increased each January 1, beginning on January 1, 2016 and thereafter until January 1, 2019, by the lesser of (i) 131,428 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, 87,368, 85,111 and 67,842 additional shares were reserved for issuance under the 2015 Plan on January 1, 2019, 2018 and 2017, respectively. In March 2019, our board of directors amended the 2015 Plan to increase the number of shares of common stock reserved under the 2015 Plan by 71,428 shares subject to approval by the Company's stockholders. At our 2019 Annual Meeting of Stockholders, our stockholders approved such amendment. Total shares available for issuance under the 2015 Plan as of January 1, 2020 were 260,999. 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 Grants**

In July 2018, we granted a non-qualified option to purchase 14,285 shares of our common stock at an exercise price of \$11.41 per share as an inducement award in connection with the hiring of our Chief Financial Officer.

Options under the inducement grants vest over a period of four 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. These options were inducement grants issued outside of the 2015 Plan in accordance with Nasdaq Listing Rule 5635(c)(4). In addition, from time to time, we may make inducement grants of stock options to new employees.

### Employee Stock Purchase Plan

In April 2015, our board of directors adopted, and our stockholders approved, our 2015 Employee Stock Purchase Plan (the 2015 ESPP). The 2015 ESPP became effective on May 6, 2015. A total of 16,258 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 automatically increased 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, 21,842, 21,277 and 16,960 additional shares were reserved for issuance under the 2015 ESPP on January 1, 2019, 2018 and 2017, respectively. As of January 1, 2020, total shares reserved for issuance under the 2015 ESPP were 78,697.

### 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
Outstanding as of December 31, 2018	356,353	\$ 62.61		
Granted	76,722	\$ 7.15		
Canceled/forfeited/expired	(81,997)	\$ 58.98		
Outstanding as of December 31, 2019	351,078	\$ 51.34	6.60	\$ 910.00
Options vested and expected to vest as of December 31, 2019	351,078	\$ 51.34	6.60	\$ 910.00
Options exercisable as of December 31, 2019	218,021	\$ 67.82	5.51	\$ 45.00

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,		
	2019	2018	2017
Expected term (in years)	5.51 – 6.07	5.00 – 6.08	5.50 – 6.08
Risk-free interest rate	1.4% – 2.6%	2.3% – 3.0%	1.9% – 2.1%
Expected volatility	97.2% – 105.4%	87.9% – 98.4%	99.1% – 124.4%
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,		
	2019	2018	2017
Expected term (in years)	0.50	0.50	0.50
Risk-free interest rate	1.6% – 2.5%	1.4% – 2.1%	0.6% – 1.0%
Expected volatility	99.7% – 141.7%	71.5% – 99.7%	74.5% – 115.2%
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.

### **Restricted Stock Units**

Occasionally, we grant restricted stock units to employees. Restricted stock unit activity is summarized as follows:

	<b>Number of Outstanding Restricted Stock Units</b>	<b>Weighted Average Grant Date Fair Value</b>
Balance as of December 31, 2018	15,470	\$ 11.91
Granted	5,356	\$ 7.24
Released	(7,487)	\$ 11.91
Forfeited	(864)	\$ 11.90
Balance as of December 31, 2019	<u>12,475</u>	<u>\$ 9.90</u>

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

	<b>Years Ended December 31,</b>		
	<b>2019</b>	<b>2018</b>	<b>2017</b>
Research and development	\$ 354	\$ 1,216	\$ 1,399
General and administrative	1,429	2,215	5,385
Total stock-based compensation expense	<u>\$ 1,783</u>	<u>\$ 3,431</u>	<u>\$ 6,784</u>

The weighted-average grant date fair value per share of stock options granted by us, during the years ended December 31, 2019, 2018 and 2017 was \$5.67, \$25.76 and \$39.95, respectively. The total grant date fair value of restricted stock units vested during the years ended December 31, 2019, 2018 and 2017 was \$39,000, \$0.2 million and \$0.1 million, respectively. The aggregate intrinsic value of stock options exercised during the years ended December 31, 2018 and 2017 was \$6,000 and \$0.3 million, respectively. We did not have any options exercised during the year ended December 31, 2019. The aggregate intrinsic value of restricted stock units released during the years ended December 31, 2019, 2018 and 2017 was \$31,000, \$19,000 and \$0.1 million. As of December 31, 2019, total unrecognized share-based compensation expense related to unvested stock options and restricted stock units was approximately \$2.4 million and \$0.1 million, respectively. These unrecognized costs for options and restricted stock units are expected to be recognized ratably over a weighted-average period of approximately 2.3 years and 0.7 years, respectively.

### **Warrants**

Warrants outstanding for the purchase of common stock as of December 31, 2019 were as follows:

<b>Number Outstanding</b>	<b>Exercise Price Per Share</b>	<b>Expiration Date</b>
144	\$ 104.65	March 2021
1,066	\$ 281.50	July 2023
6,830	\$ 43.93	November 2023
2,978	\$ 50.37	June 2024
2,886	\$ 51.98	December 2024
<u>13,904</u>		

## Common Stock Reserved for Future Issuance

Common stock reserved for future issuance was as follows:

	<u>December 31, 2019</u>
Class X Preferred Stock (if-converted to common stock)	587,445
Common stock warrants	13,904
Common stock options and restricted stock units	363,553
Shares available under the 2015 Plan	260,999
Shares available under the 2015 ESPP	78,697
	<u>1,304,598</u>

## 8. Income Tax

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

	<u>Years Ended December 31,</u>		
	<u>2019</u>	<u>2018</u>	<u>2017</u>
United States	\$ (23,315)	\$ (34,021)	\$ (47,712)
Foreign	(448)	(494)	(495)
	<u>\$ (23,763)</u>	<u>\$ (34,515)</u>	<u>\$ (48,207)</u>

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

	<u>Years Ended December 31,</u>		
	<u>2019</u>	<u>2018</u>	<u>2017</u>
Expected income taxes benefit at federal statutory rate	\$ (4,990)	\$ (7,248)	\$ (16,390)
State income taxes, net of federal benefit	(19)	(14)	(13)
Permanent items and other	750	770	1,311
Research credits	(817)	(1,222)	(2,286)
Unrecognized tax benefits	327	489	914
Foreign rate differential	20	22	87
Change in tax rate	(49)	(11)	(25)
Tax cuts and Jobs Act	—	—	27,933
Change in valuation allowance	4,778	7,214	(11,531)
Income tax (benefit) expense	<u>\$ —</u>	<u>\$ —</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 (NOLs) carryforwards, research and development credits and capitalized research and development expenses, along with other accruals and reserves. Valuation allowances of \$71.7 million and \$66.9 million as of December 31, 2019 and 2018, 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,	
	2019	2018
Deferred tax assets:		
Net operating loss carryforwards	\$ 38,180	\$ 32,997
Capitalized research and development expenses	16,900	17,279
Research credits and other state credits	12,452	11,962
Intangible assets	1,841	2,024
Reserve and accruals	2,310	2,667
Lease liability	631	—
Valuation allowance	(71,702)	(66,929)
Total deferred tax assets	\$ 612	\$ —
Deferred tax liabilities:		
Right of use lease assets	(612)	—
Total deferred tax liabilities	(612)	—
Net deferred tax assets	\$ —	\$ —

As of December 31, 2019, we had federal NOLs carryforwards of approximately \$163.7 million, with \$51.2 million of NOLs generated through December 31, 2018 carrying forward indefinitely and \$112.5 million of net NOLs that will begin to expire in 2025. NOLs generated after January 1, 2018 are subject to an 80% limitation in accordance with the Tax Cuts and Jobs Act of 2017. We had state net operating loss carryforwards of approximately \$163.3 million, and foreign net operating loss carryforwards of \$8.0 million. The state net operating losses will begin to expire in 2021. The foreign net operating losses carry over indefinitely.

As of December 31, 2019, we had federal and state research and development credit carryforwards of approximately \$5.0 million and \$4.1 million, respectively, 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, 2019, which will begin to expire in 2035.

Utilization of the domestic NOLs 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 NOLs 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 NOLs 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 NOLs or research and development credit carryforwards before utilization. We completed analyses through December 31, 2017, and are in the process of analyzing the impact to our NOLs and research and development tax credit carryforwards. During 2019 and 2018, we decided to postpone completing another Section 382 study until we start utilizing our NOLs. Due to the existence of the valuation allowance, any impact to the NOLs and research and development tax credit carryforwards from Section 382 analysis will be offset by a corresponding adjustment to valuation allowance, resulting in 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, 2019, 2018 and 2017.

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):

	<b>December 31,</b>		
	<b>2019</b>	<b>2018</b>	<b>2017</b>
Balance as of beginning of year	\$ 19,643	\$ 16,558	\$ 13,000
Increase (decrease) related to prior year tax positions	—	2	(189)
Increase related to current year tax positions	1,659	3,083	3,747
Balance as of end of year	<u>\$ 21,302</u>	<u>\$ 19,643</u>	<u>\$ 16,558</u>

We do not anticipate that the amount of unrecognized tax benefits as of December 31, 2019 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 carry forward of unutilized NOLs and research and development credits.

## 9. 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 during each of the years ended December 31, 2019, 2018 and 2017, respectively.

## 10. 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 2019 and 2018 are as follows (in thousands, except per share data):

	<b>For the quarters ended</b>			
	<b>March 31</b>	<b>June 30</b>	<b>September 30</b>	<b>December 31</b>
<b>2019:</b>				
Operating expenses	\$ 5,877	\$ 5,735	\$ 5,682	\$ 6,106
Net loss attributable to aTyr Pharma, Inc.	(6,137)	(5,848)	(5,645)	(5,973)
Basic and diluted net loss per share	\$ (2.54)	\$ (1.80)	\$ (1.47)	\$ (1.54)
<b>2018:</b>				
Operating expenses	\$ 10,220	\$ 9,960	\$ 6,677	\$ 5,963
Net loss attributable to aTyr Pharma, Inc.	(10,667)	(10,412)	(7,114)	(6,322)
Basic and diluted net loss per share	\$ (5.01)	\$ (4.88)	\$ (3.33)	\$ (2.92)

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.

## 11. Subsequent Events

In January 2020, we entered into a license with Kyorin Pharmaceutical Co., Ltd. (Kyorin) for the development and commercialization of ATYR1923 for ILDs in Japan. Under the collaboration and license agreement with Kyorin (the Kyorin Agreement), Kyorin received an exclusive right to develop and commercialize ATYR1923 in Japan for all forms of ILDs. We received an \$8.0 million upfront payment and we are eligible to receive an additional \$167.0 million in the aggregate upon achievement of certain development, regulatory and sales milestones, as well as tiered royalties ranging from the mid-single digits to mid-teens on net sales in Japan. Under the terms of the Kyorin Agreement, Kyorin will fund all research, development, regulatory, marketing and commercialization activities in Japan, as well as support our global development efforts for ATYR1923.

In January 2020, the VGO Fund converted 1,142,478 shares of its Preferred Shares into 408,247 shares of common stock and in February 2020, converted 501,483 shares of its Preferred Shares into 179,197 shares of common stock. As of February 2020, following the conversion, VGO Fund owned 6.7% of our common stock.

In February 2020, we completed an underwritten follow-on public offering of 4,235,294 shares of our common stock at a price to the public of \$4.25 per share. In March 2020, the underwriters fully exercised their over-allotment option for the issuance of an additional 635,294 shares of common stock. The total gross proceeds from the underwritten follow-on public offering, including the over-allotment, was approximately \$20.7 million, before deducting underwriting discounts, commissions and offering expenses payable by us. We anticipate using the net proceeds from the offering for general corporate purposes, including clinical trial expenses, research and development expenses, manufacturing expenses, and general administrative expenses.

In March 2020, Pangu, together with the Hong Kong University of Science and Technology (HKUST), was awarded a grant of approximately \$750,000 to build a high-throughput platform for the development of bi-specific antibodies. The two-year project is being funded by the Hong Kong Government's Innovation and Technology Commission (ITC) under the Partnership Research Program. The grant will be funded by ITC for approximately 50% of the total estimated project cost, with aTyr contributing the remaining 50%.

### 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 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, 2019.

#### Management's Report on Internal Control Over Financial Reporting

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



As of December 31, 2019, 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, 2019.

This Annual Report 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, 2019, 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 Definitive Proxy Statement to be filed with the SEC in connection with our 2020 Annual Meeting of Stockholders within 120 days after the end of the fiscal year ended December 31, 2019 (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.

**Item 15. Exhibits, Financial Statement Schedules.**

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

1. *Index list to Financial Statements:*

	<b>Page</b>
<a href="#">Report of Independent Registered Public Accounting Firm</a>	66
<a href="#">Consolidated Balance Sheets</a>	67
<a href="#">Consolidated Statements of Operations</a>	68
<a href="#">Consolidated Statements of Comprehensive Loss</a>	69
<a href="#">Consolidated Statements of Stockholders' Equity</a>	70
<a href="#">Consolidated Statements of Cash Flows</a>	71
<a href="#">Notes to Consolidated Financial Statements</a>	72

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 Annual Report.

**EXHIBIT INDEX**

<b>Exhibit Number</b>	<b>Exhibit Title</b>	<b>Form</b>	<b>Incorporated by File No.</b>	<b>Reference Exhibit</b>	<b>Filing Date</b>
3.1	<a href="#">Restated Certificate of Incorporation of the Registrant</a>	S-1/A	333-203272	3.2	May 1, 2015
3.2	<a href="#">Certificate of Amendment to Restated Certificate of Incorporation of the Registrant</a>	8-K	001-37378	3.1	June 28, 2019
3.2	<a href="#">Amended and Restated Bylaws of the Registrant</a>	S-1/A	333-203272	3.4	April 27, 2015
3.3	<a href="#">Certificate of Designation of Preferences, Rights and Limitations of Class X Convertible Preferred Stock</a>	8-K	001-37378	3.1	August 31, 2017
4.1	<a href="#">Specimen Common Stock Certificate</a>	S-1/A	333-203272	4.1	April 27, 2015
4.2	<a href="#">Warrant to Purchase Stock issued to Comerica Bank on March 18, 2011</a>	S-1	333-203272	4.3	April 6, 2015
4.3	<a href="#">Warrant to Purchase Stock issued to Silicon Valley Bank on July 24, 2013</a>	S-1	333-203272	4.4	April 6, 2015
4.4	<a href="#">Warrant to Purchase Stock issued to Silicon Valley Bank on November 18, 2016</a>	10-K	001-37378	4.5	March 16, 2017
4.5	<a href="#">Warrant to Purchase Stock issued to Solar Capital Ltd on November 18, 2016</a>	10-K	001-37378	4.6	March 16, 2017
4.6	<a href="#">Warrant to Purchase Stock issued to Silicon Valley Bank on June 30, 2017</a>	10-Q	001-37378	4.7	August 14, 2017
4.7	<a href="#">Warrant to Purchase Stock issued to Solar Capital Ltd on June 30, 2017</a>	10-Q	001-37378	4.8	August 14, 2017
4.8	<a href="#">Warrant to Purchase Stock issued to Silicon Valley Bank on December 22, 2017</a>	10-K	001-37378	4.8	March 20, 2018
4.9	<a href="#">Warrant to Purchase Stock issued to Solar Capital Ltd on December 22, 2017</a>	10-K	001-37378	4.9	March 20, 2018
4.10	<a href="#">Description of Common Stock of the Registrant</a>	—	—	—	Filed herewith
10.1#	<a href="#">2014 Stock Plan and forms of agreements thereunder</a>	S-1/A	333-203272	10.1	April 27, 2015
10.2#	<a href="#">2015 Stock Option and Incentive Plan, as amended</a>	8-K	001-37378	10.1	May 10, 2019
10.3#	<a href="#">Forms of agreement under 2015 Stock Option and Incentive Plan</a>	S-1/A	333-203272	10.2	April 27, 2015
10.4	<a href="#">Lease by and between the Registrant and BMR-John Hopkins Court LLC, dated December 22, 2011</a>	S-1	333-203272	10.9	April 6, 2015
10.5	<a href="#">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</a>	10-K	001-37378	10.8	March 16, 2017
10.6	<a href="#">Form of Indemnification Agreement entered into between the Registrant and its directors</a>	S-1/A	333-203272	10.12	April 27, 2015
10.7	<a href="#">Form of Indemnification Agreement entered into between the Registrant and its officers</a>	S-1/A	333-203272	10.13	April 27, 2015
10.8#	<a href="#">2015 Employee Stock Purchase Plan</a>	S-1/A	333-203272	10.14	April 27, 2015
10.9#	<a href="#">Senior Executive Cash Incentive Bonus Plan</a>	8-K	001-37378	10.1	January 29, 2016
10.10#	<a href="#">Executive Severance and Change in Control Policy</a>	10-K	001-37378	10.16	March 30, 2016

Exhibit Number	Exhibit Title	Form	Incorporated by Reference File No.	Exhibit	Filing Date
10.11#	<a href="#">Registrant's Non-Qualified Stock Option Agreement for Non-Plan Inducement Grant</a>	10-Q	001-37378	10.1	November 14, 2016
10.12†	<a href="#">Loan and Security Agreement by and between the Registrant and Silicon Valley Bank and Solar Capital Ltd, dated November 18, 2016</a>	10-K	001-37378	10.17	March 16, 2017
10.13	<a href="#">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</a>	10-Q	001-37378	10.1	May 11, 2017
10.14	<a href="#">First Amendment to Loan and Security Agreement between the Registrant and Silicon Valley Bank and Solar Capital Ltd, dated June 30, 2017</a>	10-Q	001-37378	10.1	August 14, 2017
10.15#	<a href="#">Employment Agreement, dated November 1, 2017, by and between the Company and Sanjay S. Shukla, M.D., M.S.</a>	10-Q	001-37378	10.4	November 14, 2017
10.16	<a href="#">Second Amendment to Loan and Security Agreement between the Registrant and Silicon Valley Bank and Solar Capital Ltd, dated October 10, 2017</a>	10-K	001-37378	10.21	March 20, 2018
10.17	<a href="#">Third Amendment to Loan and Security Agreement between the Registrant and Silicon Valley Bank and Solar Capital Ltd, dated December 22, 2017</a>	10-K	001-37378	10.23	March 20, 2018
10.18#	<a href="#">Employment Offer Letter by and between the Registrant and Jill M. Broadfoot, dated July 16, 2018</a>	8-K	001-37378	10.1	August 1, 2018
10.19	<a href="#">Third Amendment to Lease between Registrant and BMR-3545-3575 John Hopkins LP (as successor-in interest to BMR-John Hopkins Court, LLC), dated July 30, 2018</a>	10-Q	001-37378	10.1	November 11, 2018
10.20#	<a href="#">Employment Offer Letter by and between Registrant and Ms. Nancy Krueger, Esq., dated October 7, 2014</a>	10-Q	001-37378	10.2	May 14, 2019
10.21†	<a href="#">Collaboration and License Agreement by and between Registrant and Kyorin Pharmaceutical Co., Ltd. agreement, dated January 6, 2020</a>	S-1/A	333-235951	10.21	February 3, 2020
10.22	<a href="#">Common Stock Sales Agreement, between the Registrant and H.C. Wainwright &amp; Co., LLC, dated May 21, 2019</a>	8-K	001-37378	10.1	May, 22, 2019
10.23	<a href="#">Amendment No. 1 to Common Stock Sales Agreement, dated June 18, 2019, between the Registrant and H.C. Wainwright &amp; Co., LLC</a>	S-3/A	333-231658	1.3	June 18, 2019
14.1	<a href="#">Code of Business Conduct and Ethics</a>	10-Q	001-37378	14.1	June 18, 2015
21.1	<a href="#">Subsidiaries of the Registrant</a>	S-1	333-203272	21.1	April 6, 2015
23.1	<a href="#">Consent of Independent Registered Public Accounting Firm</a>	—	—	—	Filed herewith
24.1	<a href="#">Power of Attorney (included on signature page to this Annual Report)</a>	—	—	—	Filed herewith
31.1	<a href="#">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</a>	—	—	—	Filed herewith
31.2	<a href="#">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</a>	—	—	—	Filed herewith
32.1	<a href="#">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</a>	—	—	—	Filed herewith
32.2	<a href="#">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</a>	—	—	—	Filed herewith

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

† Certain portions have been omitted because the Registrant has determined that the information is not material and would likely cause competitive harm to the Registrant if publicly disclosed.

**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 26, 2020

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, M.D., M.S. and Jill M. Broadfoot, 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.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ Sanjay S. Shukla</u> Sanjay S. Shukla, M.D., M.S.	President, Chief Executive Officer and Director (Principal Executive Officer)	March 26, 2020
<u>/s/ Jill M. Broadfoot</u> Jill M. Broadfoot	Chief Financial Officer (Principal Financial and Accounting Officer)	March 26, 2020
<u>/s/ John K. Clarke</u> John K. Clarke	Chairman of the Board	March 26, 2020
<u>/s/ James C. Blair</u> James C. Blair, Ph.D.	Director	March 26, 2020
<u>/s/ Timothy P. Coughlin</u> Timothy P. Coughlin	Director	March 26, 2020
<u>/s/ Jane A. Gross</u> Jane A. Gross, Ph.D.	Director	March 26, 2020
<u>/s/ Jeffrey S. Hatfield</u> Jeffrey S. Hatfield	Director	March 26, 2020
<u>/s/ Svetlana Lucas</u> Svetlana Lucas, Ph.D.	Director	March 26, 2020
<u>/s/ Paul Schimmel</u> Paul Schimmel, Ph.D.	Director	March 26, 2020

## DESCRIPTION OF COMMON STOCK

The following summary description of the common stock of aTyr Pharma, Inc. (we, our or us) is based on the provisions of our amended and restated certificate of incorporation, as well as our amended and restated bylaws, and the applicable provisions of the Delaware General Corporation Law (DGCL). This information is qualified entirely by reference to the applicable provisions of our amended and restated certificate of incorporation, amended and restated bylaws, and the DGCL. Our amended and restated certificate of incorporation and amended and restated bylaws have previously been filed as exhibits with the Securities and Exchange Commission (SEC).

### Common Stock

The holders of our common stock are entitled to one vote for each share held on all matters submitted to a vote of the stockholders. The holders of our common stock do not have any cumulative voting rights. Holders of our common stock are entitled to receive ratably any dividends declared by our Board of Directors out of funds legally available for that purpose, subject to any preferential dividend rights of any outstanding preferred stock. Our common stock has no preemptive rights, conversion rights or other subscription rights or redemption or sinking fund provisions.

In the event of our liquidation, dissolution or winding up, holders of our common stock will be entitled to share ratably in all assets remaining after payment of all debts and other liabilities and any liquidation preference of any outstanding preferred stock.

### Preferred Stock

The rights of holders of our common stock described above, are and will be subject to, and may be adversely affected by, the rights of currently authorized and outstanding preferred stock and any preferred stock that we may designate and issue in the future. Our Board of Directors is authorized to issue up to 2,714,048 shares of undesignated preferred stock in one or more series without stockholder approval. Our Board of Directors may determine the rights, preferences, privileges and restrictions, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences, of each series of preferred stock, any or all of which may be more favorable than the rights of our common stock. The issuance of shares of undesignated preferred stock could decrease the amount of earnings and assets available for distribution to holders of shares of common stock. The issuance may also adversely affect the rights and powers, including voting rights, of these holders and may have the effect of delaying, deterring or preventing a change in control of us. The existence of authorized but unissued shares of undesignated preferred stock may enable our Board of Directors to render more difficult or to discourage an attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise. For example, if in the due exercise of its fiduciary obligations, our Board of Directors were to determine that a takeover proposal is not in the best interests of us or our stockholders, our Board of Directors could cause shares of preferred stock to be issued without stockholder approval in one or more private offerings or other transactions that might dilute the voting or other rights of the proposed acquirer, stockholder or stockholder group.

Our Board of Directors is authorized to issue up to 5,000,000 shares of undesignated preferred stock in one or more series without stockholder approval. Our Board of Directors may determine the rights, preferences, privileges and restrictions, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences, of each series of preferred stock, any or all of which may be more favorable than the rights of our common stock.

## **Provisions of our Amended and Restated Certificate of Incorporation and Amended and Restated Bylaws and Delaware Anti-Takeover Law**

Certain provisions of the DGCL and of our amended and restated certificate of incorporation and amended and restated bylaws could have the effect of delaying, deferring or discouraging another party from acquiring control of us. These provisions, which are summarized below, are expected to discourage certain types of coercive takeover practices and inadequate takeover bids and, as a consequence, they might also inhibit temporary fluctuations in the market price of our common stock that often result from actual or rumored hostile takeover attempts. These provisions are also designed in part to encourage anyone seeking to acquire control of us to first negotiate with our Board of Directors. These provisions might also have the effect of preventing changes in our management. It is possible that these provisions could make it more difficult to accomplish transactions that stockholders might otherwise deem to be in their best interests. However, we believe that the advantages gained by protecting our ability to negotiate with any unsolicited and potentially unfriendly acquirer outweigh the disadvantages of discouraging such proposals, including those priced above the then-current market value of our common stock, because, among other reasons, the negotiation of such proposals could improve their terms.

**Board Composition and Filling Vacancies.** Our amended and restated certificate of incorporation provides for the division of our Board of Directors into three classes serving staggered three-year terms, with one class being elected each year. Our amended and restated certificate of incorporation also provides that directors may be removed only for cause and then only by the affirmative vote of the holders of 75% or more of the shares then entitled to vote at an election of directors. Furthermore, any vacancy on our Board of Directors, however occurring, including a vacancy resulting from an increase in the size of our board, may only be filled by the affirmative vote of a majority of our directors then in office even if less than a quorum.

**No Written Consent of Stockholders.** Our amended and restated certificate of incorporation provides that all stockholder actions are required to be taken by a vote of the stockholders at an annual or special meeting, and that stockholders may not take any action by written consent in lieu of a meeting.

**Meetings of Stockholders.** Our amended and restated certificate of incorporation and amended and restated bylaws provide that only a majority of the members of our Board of Directors then in office may call special meetings of stockholders and only those matters set forth in the notice of the special meeting may be considered or acted upon at a special meeting of stockholders. Our amended and restated bylaws limit the business that may be conducted at an annual meeting of stockholders to those matters properly brought before the meeting.

**Advance Notice Requirements.** Our amended and restated bylaws establish advance notice procedures with regard to stockholder proposals relating to the nomination of candidates for election as directors or new business to be brought before meetings of our stockholders. These procedures provide that notice of stockholder proposals must be timely given in writing to our corporate secretary prior to the meeting at which the action is to be taken.

**Amendment to Amended and Restated Certificate of Incorporation and Amended and Restated Bylaws.** As required by the DGCL, any amendment of our amended and restated certificate of incorporation must first be approved by a majority of our Board of Directors, and if required by law or our amended and restated certificate of incorporation, must thereafter be approved by a majority of the outstanding shares entitled to vote on the amendment and a majority of the outstanding shares of each class entitled to vote thereon as a class, except that the amendment of the provisions relating to stockholder action, board composition, limitation of liability and the amendment of our certificate of incorporation must be approved



by not less than 75% of the outstanding shares entitled to vote on the amendment, and not less than 75% of the outstanding shares of each class entitled to vote thereon as a class. Our amended and restated bylaws may be amended by the affirmative vote of a majority of the directors then in office, subject to any limitations set forth in the amended and restated bylaws; and may also be amended by the affirmative vote of at least 75% of the outstanding shares entitled to vote on the amendment, or, if our Board of Directors recommends that the stockholders approve the amendment, by the affirmative vote of the majority of the outstanding shares entitled to vote on the amendment, in each case voting together as a single class.

**Delaware Anti-Takeover Law.** We are subject to the provisions of Section 203 of the DGCL. In general, Section 203 prohibits a publicly held Delaware corporation from engaging in a “business combination” with an “interested stockholder” for a three-year period following the time that this stockholder becomes an interested stockholder, unless the business combination is approved in a prescribed manner. Under Section 203, a business combination between a corporation and an interested stockholder is prohibited unless it satisfies one of the following conditions:

- before the stockholder became interested, the board of directors approved either the business combination or the transaction which resulted in the stockholder becoming an interested stockholder;
- upon consummation of the transaction which resulted in the stockholder becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding for purposes of determining the voting stock outstanding, shares owned by persons who are directors and also officers, and employee stock plans, in some instances; or
- at or after the time the stockholder became interested, the business combination was approved by the board of directors of the corporation and authorized at an annual or special meeting of the stockholders by the affirmative vote of at least two-thirds of the outstanding voting stock which is not owned by the interested stockholder.

Section 203 defines a business combination to include:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, lease, pledge or other disposition involving the interested stockholder of 10% or more of the assets of the corporation;
- subject to exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder;
- subject to exceptions, any transaction involving the corporation that has the effect of increasing the proportionate share of the stock of any class or series of the corporation beneficially owned by the interested stockholder; and
- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

In general, Section 203 defines an interested stockholder as any entity or person beneficially owning or having owned in the past three years 15% or more of the outstanding voting stock of the corporation and any entity or person affiliated with or controlling or controlled by the entity or person.

***Exclusive Jurisdiction of Certain Actions.*** Our amended and restated bylaws provide that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware shall be the sole and exclusive forum for (i) any derivative action or proceeding brought on our behalf, (ii) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers or other employees to us or our stockholders, (iii) any action asserting a claim arising pursuant to any provision of the DGCL, our amended and restated certificate of incorporation or our amended and restated bylaws, or (iv) any action asserting a claim against us governed by the internal affairs doctrine. Although we believe this provision benefits us by providing increased consistency in the application of Delaware law in the types of lawsuits to which it applies, the provision may have the effect of discouraging lawsuits against our directors and officers. This choice of forum provision does not apply to suits brought to enforce a duty or liability created by the Securities Act of 1933, as amended, or the Exchange Act, or any other claim for which the federal courts have exclusive jurisdiction.

This choice of forum provision may limit a stockholder's ability to bring certain claims in a judicial forum that it finds favorable for disputes with us or any of our directors, officers, other employees or stockholders, which may discourage lawsuits with respect to such claims, although our stockholders will not be deemed to have waived our compliance with federal securities laws and the rules and regulations thereunder. If a court were to find this choice of forum provision to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could adversely affect our business and financial condition.

#### **Listing**

Our common stock is listed on the Nasdaq Capital Market under the symbol "LIFE."

#### **Transfer Agent and Registrar**

The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company, LLC. The transfer agent and registrar's address is 6201 15th Avenue, Brooklyn, NY 11219.

**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. 333-220463 and 333-231658) 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 Statements (Form S-8 Nos. 333-210543 and 333-223865) 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 Statements (Form S-8 Nos. 333-216880 and 333-231594) 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 26, 2020, with respect to the consolidated financial statements of aTyr Pharma, Inc. included in this Annual Report (Form 10-K) of aTyr Pharma, Inc. for the year ended December 31, 2019.

/s/ Ernst & Young LLP  
San Diego, California  
March 26, 2020

**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 26, 2020

/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, Jill M. Broadfoot, 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 26, 2020

/s/ Jill M. Broadfoot

Jill M. Broadfoot

Chief Financial Officer

(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, 2019, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Sanjay S. Shukla, President and Chief Executive Officer of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to my knowledge:

1. The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and
2. The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 26, 2020

/s/ Sanjay S. Shukla

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

The foregoing certification is being furnished solely to accompany the Report pursuant to 18 U.S.C. § 1350, and is not being filed for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, and is not to be incorporated by reference into any filing of the Company, whether made before or after the date hereof, regardless of any general incorporation language in such filing. A signed original of this written statement required by Section 906 has been provided to the Company and will be retained by the Company and furnished to the Securities and Exchange Commission or its staff upon request.

**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, 2019, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Jill M. Broadfoot, Chief Financial 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 26, 2020

/s/ Jill M. Broadfoot

Jill M. Broadfoot

Chief Financial Officer

(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.