

PROSPECTUS



**4,235,294 Shares of Common Stock**

We are offering 4,235,294 shares of our common stock. Our common stock is listed on the Nasdaq Capital Market under the symbol "LIFE". The last reported sale price of our common stock on the Nasdaq Capital Market on February 5, 2020 was \$4.51 per share.

We are an "emerging growth company" as defined by the Jumpstart Our Business Startups Act of 2012, and as such, we have elected to comply with certain reduced public company reporting requirements for this prospectus and future filings.

**Investing in our securities involves a high degree of risk. See "[Risk Factors](#)" beginning on page 8 of this prospectus to read about factors you should consider before buying our securities.**

	Per Share	Total
Public offering price	\$ 4.25	\$ 18,000,000
Underwriting discounts and commissions (1)	\$ 0.2975	\$ 1,260,000
Proceeds, before expenses, to aTyr Pharma, Inc.	\$ 3.9525	\$ 16,740,000

(1) See "Underwriting" for additional information regarding underwriting compensation.

We have granted the underwriters an option to purchase up to an additional 635,294 shares of our common stock, solely to cover over-allotments, if any.

The underwriters expect to deliver the shares to purchasers against payment on or about February 10, 2020.

**Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.**

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*Sole Book-Running Manager*

**Oppenheimer & Co.**

*Lead Manager*

**Roth Capital Partners**

**The date of this prospectus is February 5, 2020**

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We have not, and the underwriters have not, authorized anyone to provide you with any information or to make any representation other than that contained in this prospectus or in any free writing prospectuses prepared by or on behalf of us or to which we have referred you. We do not, and the underwriters do not, take any responsibility for, and can provide no assurance as to the reliability of, any information that others may provide to you. This prospectus is not an offer to sell or an offer to buy these securities in any jurisdiction where offers and sales are not permitted. The information in this prospectus is accurate only as of its date, regardless of the time of delivery of this prospectus or any sale of securities. You should also read and consider the information in the documents to which we have referred you under the caption "Where You Can Find More Information" in this prospectus.

Neither we nor the underwriters have done anything that would permit a public offering of the securities or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than in the United States. Persons outside the United States who come into possession of this prospectus must inform themselves about, and observe any restrictions relating to, the offering of the securities and the distribution of this prospectus outside of the United States.

## PROSPECTUS SUMMARY

*The following summary highlights information contained elsewhere in this prospectus and does not contain all of the information that you should consider in making your investment decision. Before investing in our securities, you should carefully read this entire prospectus, including the sections in this prospectus entitled “Risk Factors,” “Management’s Discussion and Analysis of Financial Condition and Results of Operations”, and our consolidated financial statements and the related notes included elsewhere in this prospectus, before making an investment decision.*

*Except as otherwise indicated herein or as the context otherwise requires, references in this prospectus to “aTyr,” the “company,” “we,” “us” and “our” refer to aTyr Pharma, Inc., together with our subsidiary, Pangu BioPharma Limited.*

### Company 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.

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 (CSL Agreement). Under the terms of the collaboration, CSL is obligated to fund all research and development activities and to 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.

## Our Therapeutic Candidate Pipeline

PROGRAM	DISEASES	DISCOVERY	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3	PARTNERS
	Pulmonary Sarcoidosis						
ATYR1923	Chronic Hypersensitivity Pneumonitis (CHP)						Kyorin ILD in Japan
	Connective Tissue Disease ILD (CTD-ILD)						
tRNA synthetase candidates	Immunology						CSL Behring 4 synthetases
NRP2 antibodies	Cancer; Inflammation						

## Financial Update

Our financial statements for the fiscal year ended December 31, 2019 will not be available until after this offering is completed, and consequently will not be available to you prior to investing in this offering.

## Risks Associated with Our Business

Investing in our securities involves substantial risk. The risks described under the heading “Risk Factors” immediately following this summary may cause us to not realize the full benefits of our strengths or may cause us to be unable to successfully execute all or part of our strategy. Some of the more significant challenges include the following:

- We will need to raise additional capital or enter into strategic partnering relationships to fund our operations.
- We have a significant amount of debt that may cause risks that could adversely affect our business, operating results and financial condition.
- We have incurred significant losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future.
- 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.
- 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.
- 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.
- 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.

- 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.
- 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.
- Our future success depends on our ability to retain key employees, consultants and advisors and to attract, retain and motivate qualified personnel.
- Our executive officers, directors, principal stockholders 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.

### **Corporate Information**

We were incorporated under the laws of the State of Delaware in September 2005. In October 2007, we formed our Hong Kong subsidiary, Pangu BioPharma Limited (Pangu BioPharma). We hold 98% of the outstanding shares of Pangu BioPharma, and a subsidiary of the Hong Kong University of Science and Technology holds the remaining outstanding shares.

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) and we regularly post copies of our press release as well as additional information about us on our website.

Our design logo, “aTyr,” and our other registered and common law trade names, trademarks and service marks are the property of aTyr Pharma, Inc.

The trademarks, trade names and service marks appearing in this prospectus are the property of their respective owners. We do not intend our use or display of other companies’ trademarks, trade names or service marks to imply a relationship with, or endorsement or sponsorship of us by, any other companies or products.

### **Implications of Being an Emerging Growth Company and Smaller Reporting Company**

We are an emerging growth company, as defined in the Jumpstart Our Business Startups Act of 2012 (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 of 2002, or the Sarbanes-Oxley Act, reduced disclosure obligations regarding executive compensation in this prospectus and our periodic reports and proxy statements and exemptions from the requirements of holding nonbinding advisory votes 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 reduced disclosure obligations regarding executive compensation in our periodic reports and proxy statements. Additionally, even if we no longer qualify as an emerging growth company, as long as we are neither a “large accelerated filer” nor an “accelerated filer,” we would not be required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act.

We cannot predict if investors will find our securities less attractive because we may rely on these exemptions, which could result in a less active trading market for our securities and increased volatility in the price of our securities.

Finally, we are a “smaller reporting company” (and may continue to qualify as such even after we no longer qualify as an emerging growth company) and accordingly may provide less public disclosure than larger public companies, including the inclusion of only two years of audited financial statements and only two years of related selected financial data and management’s discussion and analysis of financial condition and results of operations disclosure. As a result, the information that we provide to our stockholders may be different than you might receive from other public reporting companies in which you hold equity interests.

## THE OFFERING

<b>Common stock to be offered by us</b>	4,235,294 shares
<b>Common stock to be outstanding after this offering</b>	8,125,479 shares (or 8,760,773 shares if the underwriters exercise their over-allotment option in full)
<b>Underwriters' over-allotment option</b>	We have granted the underwriters the option to purchase up to an additional 635,294 shares of our common stock, solely to cover over-allotments, if any. The underwriters can exercise this option at any time within 30 days after the date of this prospectus.
<b>Use of proceeds</b>	<p>We estimate that the net proceeds to us from this offering will be approximately \$16.2 million, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.</p> <p>We intend to use the net proceeds from this offering primarily for general corporate purposes, including clinical trial expenses, research and development expenses, manufacturing expenses, and general and administrative expenses. See "Use of Proceeds" for additional information.</p>
<b>Risk factors</b>	An investment in our securities involves a high degree of risk. See "Risk Factors" and the other information included in this prospectus for a discussion of factors you should carefully consider before deciding to invest in our common stock.
<b>Nasdaq Capital Market symbol</b>	"LIFE"

Except as otherwise indicated herein, the number of shares of common stock to be outstanding after this offering is based on 3,890,185 shares of common stock outstanding as of September 30, 2019 and excludes:

- 389,706 shares of common stock issuable upon the exercise of stock options outstanding as of September 30, 2019, with a weighted average exercise price of \$51.35 per share;
- 12,832 shares of common stock issuable upon the vesting and settlement of restricted stock units outstanding as of September 30, 2019;
- 477,639 shares of common stock issuable upon the exercise of warrants outstanding as of September 30, 2019, with a weighted average exercise price of \$64.95 per share;
- 222,014 shares of common stock reserved for future issuance under our 2015 Stock Option and Incentive Plan (2015 Plan) as of September 30, 2019;
- 80,299 shares of common stock reserved for future issuance under our 2015 Employee Stock Purchase Plan (ESPP) as of September 30, 2019; and
- 587,445 shares of common stock issuable upon the conversion of 1,643,961 shares of Class X Convertible Preferred Stock outstanding as of September 30, 2019.

Unless otherwise indicated, all information contained in this prospectus assumes:

- no expiration of warrants to purchase 463,735 shares of common stock which expired pursuant to their respective terms as of December 31, 2019;
- no exercise of the outstanding options or warrants described above;

- no conversion of the outstanding shares of Class X Convertible Preferred Stock described above, including the 408,247 shares of common stock that were issued upon conversion of 1,142,478 shares of Class X Convertible Preferred Stock in January 2020; and
- no exercise by the underwriters of their over-allotment option.

Paul Schimmel, Ph.D., a stockholder and member of our Board of Directors, has indicated an interest in purchasing up to a number of shares of the common stock offered in this offering as would maintain his current pro-rata percentage ownership of our common stock. Because indications of interest are not binding agreements or commitments to purchase, he may determine to purchase fewer or more shares than he has indicated an interest in purchasing, or elect not to purchase any shares in this offering. The underwriters may also determine to sell fewer, more or no shares in this offering to him.

## SUMMARY CONSOLIDATED FINANCIAL DATA

The following tables set forth our summary historical consolidated financial data as of, and for the periods ended on, the dates indicated. The summary consolidated statements of operations data for the years ended December 31, 2017 and 2018 are derived from our audited consolidated financial statements and notes that are included elsewhere in this prospectus. The summary consolidated statements of operations data for the nine months ended September 30, 2018 and 2019 and the summary consolidated balance sheets data as of September 30, 2019 are derived from our unaudited interim consolidated financial statements and notes that are included elsewhere in this prospectus. We have prepared the unaudited consolidated financial statements in accordance with generally accepted accounting principles (GAAP) and on the same basis as the audited consolidated financial statements, except for the impact of the adoption of ASU 2016-02, *Leases*, and have included all adjustments, consisting of only normal recurring adjustments that, in our opinion, we consider necessary for a fair statement of the consolidated financial information set forth in those statements. Our historical results are not necessarily indicative of our results in any future period and results from our interim period may not necessarily be indicative of the results of the entire year.

The following summary consolidated financial data should be read together with the information under the caption “Management’s Discussion and Analysis of Financial Condition and Results of Operations” and our audited and interim unaudited consolidated financial statements and related notes appearing elsewhere in this prospectus. The summary consolidated financial data in this section are not intended to replace our audited and interim unaudited consolidated financial statements and the related notes and are qualified in their entirety by the audited and interim unaudited consolidated financial statements and related notes included elsewhere in this prospectus.

	<b>Years Ended</b>		<b>Nine Months Ended September 30,</b>	
	<b>December 31,</b>		<b>2019</b>	
	<b>2018</b>	<b>2017</b>	<b>2019</b>	<b>2018</b>
	<b>(in thousands, except share and per share data)</b>		<b>(in thousands, except share and per share data) (unaudited)</b>	
<b>Consolidated Statements of Operations Data:</b>				
Revenues:				
Collaboration revenue	\$ —	\$ —	\$ 278	\$ —
Total revenues	—	—	278	—
Operating expenses:				
Research and development	20,385	30,067	10,458	16,836
General and administrative	12,435	17,078	6,836	10,021
Total operating expenses	32,820	47,145	17,294	26,857
Loss from operations	(32,820)	(47,145)	(17,016)	(26,857)
Total other income (expense), net	(1,695)	(1,062)	(614)	(1,336)
Net loss	\$ (34,515)	\$ (48,207)	\$ (17,630)	\$ (28,193)
Net loss per share attributable to common stock holders, basic and diluted (1)	\$ (16.11)	\$ (26.13)	\$ (5.55)	\$ (13.22)
Weighted average common stock shares outstanding, basic and diluted (1)	2,141,961	1,845,033	3,175,177	2,133,055

(1) See Note 1 to our audited and interim unaudited consolidated financial statements and related notes included elsewhere in this prospectus for a description of how we compute basic and diluted net loss per share attributable to common stockholders.



As of September 30, 2019

	Actual	As Adjusted(1)
	(unaudited) (in thousands)	
<b>Consolidated Balance Sheets Data:</b>		
Cash, cash equivalents and investments	\$ 38,064	\$ 54,304
Working capital(2)	27,316	43,556
Total assets	43,745	59,985
Current portion of operating lease liability	729	729
Long-term operating lease liability, net of current portion	2,439	2,439
Current portion of long-term loans	7,844	7,844
Long-term portion of term loans, net of current portion and debt issuance costs and discount	2,742	2,742
Total stockholders' equity	26,736	42,976

- (1) The as adjusted column reflects the receipt of the net proceeds from the sale of 4,235,294 shares of our common stock by us in this offering at the public offering price of \$4.25 per share, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.
- (2) We define working capital as current assets less current liabilities. See our interim unaudited consolidated financial statements and related notes included elsewhere in this prospectus for further details regarding our current assets and current liabilities.

## RISK FACTORS

*An investment in our securities involves a high degree of risk. You should carefully consider the risks described below and all of the other information contained in this prospectus and in any free writing prospectuses prepared by or on behalf of us or to which we have referred you, including our consolidated financial statements and the related notes and “Management’s Discussion and Analysis of Financial Condition and Results of Operations” before deciding whether to invest in our securities. If any of the possible events described below actually occur, our business, business prospects, cash flow, results of operations or financial condition could be harmed. In this case, the trading price of our common stock could decline, and you might lose all or part of your investment.*

*The following is a discussion of the risk factors that we believe are material to us at this time. These risks and uncertainties are not the only ones facing us and there may be additional matters that we are unaware of or that we currently consider immaterial. All of these could adversely affect our business, results of operations, financial condition and cash flows.*

### **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 September 30, 2019, our cash, cash equivalents and investments were approximately \$38.1 million. We expect that our existing cash, cash equivalents and investments will be sufficient to meet our anticipated cash requirements for a period of at least one year from the date of this prospectus. 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 September 30, 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 \$9.3 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 net losses of \$17.6 million and \$28.2 million for the nine months ended September 30, 2019 and 2018, respectively. As of September 30, 2019, we had an accumulated deficit of \$316.3 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 U.S. Food and Drug Administration (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 contract research organization (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 fluorodeoxyglucose-positron emission tomography (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 immuno-modulation and tissue regeneration have not been studied extensively, nor has the safety of this class of protein therapeutics been evaluated extensively in humans. The therapeutic product candidates that we elect to develop may not have the physiological functions that we currently ascribe to them, may have limited or no therapeutic applications, or may present safety problems of which we are not yet aware. We cannot be sure that our discovery engine will yield therapeutic product candidates that are safe, effective, approvable by regulatory authorities, manufacturable, scalable, or profitable.

Because our work 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 Good Manufacturing Practices (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 immuno-modulatory activity or therapeutic effects, if any, of our product candidates in patients.***

Our scientists discovered the Resokine pathway using *in vivo* screening systems designed to test potential immuno-modulatory activity in animal models of severe immune activity or inflammation, combined with data relating to the potential blockade of the Resokine pathway in a population of patients with myopathy that occurs in a particular rare disease, anti-synthetase syndrome, with Jo-1 antibodies. Translational medicine, or the application of basic scientific findings to develop therapeutics that promote human health, is subject to a number of inherent risks. In particular, scientific hypotheses formed from 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 pharmacokinetics (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 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 Collaboration 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 investigational new drug application (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 United States Patent and Trademark Office (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 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 U.S. Foreign Corrupt Practices Act (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, 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. To the extent that any disruption or security breach were to result in a loss of or damage to our data, 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 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 prospectus, 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 a BLA or IND for any of our product candidates and any adverse development or perceived adverse development with respect to the FDA's review of that BLA or IND;
- 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 January 10, 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 45.9% 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 April 2019, we entered into a securities purchase agreement and sold 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. 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, 2018, we had federal net operating loss (NOL) carryforwards of approximately \$139.5 million, with \$27.0 million of NOL generated after December 31, 2017 carrying forward indefinitely and \$112.5 million of NOL that will begin to expire

in 2025. We had state NOL carryforwards of approximately \$148.2 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.

### **Risks Related to This Offering**

***If you purchase our securities in this offering, you may incur immediate and substantial dilution in the book value of your shares. You will experience further dilution if we issue additional equity or equity-linked securities in the future.***

The public offering price per share of our common stock may be substantially higher than the net tangible book value per share of our common stock immediately prior to the offering. After giving effect to the sale of 4,235,294 shares of our common stock in this offering, at the public offering price of \$4.25 per share, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, purchasers of our common stock in this offering will have paid \$1.04 less than the as adjusted net tangible book value of the common stock value per share after this offering. For a further description of the dilution that investors in this offering may experience, see "Dilution."

If we issue additional shares of common stock (including pursuant to the exercise of outstanding stock options or warrants or the vesting and settlement of restricted stock units), or securities convertible into or exchangeable or exercisable for shares of common stock, our stockholders, including investors who purchase shares of common stock in this offering, will experience additional dilution, and any such issuances may result in downward pressure on the price of our common stock. We also cannot assure you that we will be able to sell shares or other securities in any other offering at a price per share that is equal to or greater than the price per share paid by investors in this offering, and investors purchasing shares or other securities in the future could have rights superior to existing stockholders.

***We have broad discretion in the use of the net proceeds we receive from this offering and may not use them effectively.***

Our management will have broad discretion in the application of the net proceeds we receive in this offering, including for any of the purposes described in the section entitled "Use of Proceeds," and you will not have the opportunity as part of your investment decision to assess whether our management is using the net proceeds appropriately. Because of the number and variability of factors that will determine our use of our net proceeds from this offering, their ultimate use may vary substantially from their currently intended use. The failure by our management to apply these funds effectively could result in financial losses that could have a material adverse effect on our business and cause the price of our common stock to decline. Pending their use, we may invest our net proceeds from this offering in short-term, investment-grade, interest-bearing securities. These investments may not yield a favorable return to our stockholders.



## SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Securities Exchange Act of 1934, as amended (the Exchange Act). Any statements about our expectations, beliefs, plans, objectives, assumptions or future events or performance are not historical facts and may be forward-looking. These statements are often, but are not always, made through the use of words or phrases such as “may,” “will,” “could,” “should,” “expects,” “intends,” “plans,” “anticipates,” “believes,” “estimates,” “predicts,” “projects,” “potential,” “continue,” and similar expressions, or the negative of these terms, or similar expressions. Accordingly, these statements involve estimates, assumptions, risks and uncertainties which could cause actual results to differ materially from those expressed in them. Any forward-looking statements are qualified in their entirety by reference to the factors discussed throughout this prospectus, and in particular those factors referenced in the section “Risk Factors.”

This prospectus contains forward-looking statements that are based on our management’s belief and assumptions and on information currently available to our management. These statements relate to future events or our future financial performance, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from any future results, levels of activity, performance or achievements expressed or implied by these forward-looking statements. Moreover, we operate in a very competitive and rapidly changing environment. New risks emerge from time to time. It is not possible for our management to predict all risks, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements we may make. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Forward-looking statements include, but are not limited to, statements about:

- the success, cost and timing of our clinical trials and whether the results of our trials will be sufficient to support U.S. or foreign regulatory approvals;
- whether our existing capital resources will be sufficient to enable us to complete any particular portion of our planned clinical development of our product candidates or support our operations through particular time periods;
- the potential benefits of our collaborations with Kyorin and CSL;
- the likelihood and timing of regulatory approvals for our product candidates;
- our ability to identify and discover additional product candidates;
- our ability to obtain, maintain, defend and enforce intellectual property rights protecting our product candidates;
- our estimates of our expenses, ongoing losses, future revenue, capital requirements and our needs for or ability to obtain additional financing;
- the performance of third-party service providers and independent contractors upon whom we rely to conduct our clinical trial and to manufacture our product candidates or certain components of our product candidates;
- our ability to develop sales and marketing capabilities or to enter into strategic partnerships to develop and commercialize our product candidates;
- the timing and success of the commercialization of our product candidates;
- the rate and degree of market acceptance of our product candidates;
- the size and growth of the potential markets for our product candidates and our ability to serve those markets;
- regulatory developments in the United States and foreign countries;
- the success of competing therapies that are or may become available;
- our ability to attract and retain key scientific, medical or management personnel; and
- other risks and uncertainties, including those described under the section entitled “Risk Factors” herein.

These forward-looking statements are neither promises nor guarantees of future performance due to a variety of risks and uncertainties, many of which are beyond our control, which could cause actual results to differ materially from those indicated by these forward-looking statements, including, without limitation: the possibility that we may experience slower than expected clinical site initiation or slower than expected identification and enrollment of evaluable patients; the potential for delays or problems in analyzing data or the need for additional analysis, data or patients; the potential that future pre-clinical and clinical results may not support further development of our product candidates; the potential for unexpected adverse events in the conduct of one of our clinical trials to impact our ability to continue the clinical trial or further development of a product candidate; the risk that we may encounter other unexpected hurdles or issues in the development and manufacture of our product candidates that may impact our cost, timing or progress, as well as those risks more fully discussed in the “Risk Factors” section.

Given these uncertainties, readers should not place undue reliance on our forward-looking statements. These forward-looking statements speak only as of the date on which the statements were made and are not guarantees of future performance. Except as may be required by applicable law, we do not undertake to update any forward-looking statements after the date of this prospectus.

## USE OF PROCEEDS

We estimate that the net proceeds to us from this offering will be approximately \$16.2 million, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters exercise their over-allotment option in full, we estimate that our net proceeds will be approximately \$18.7 million, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

We intend to use net proceeds from this offering for general corporate purposes, including clinical trial expenses, research and development expenses, manufacturing expenses and general and administrative expenses. The timing and amount of our actual expenditures will be based on many factors, including cash flows from operations and the anticipated growth of our business. We have not yet determined the amount of net proceeds to be used specifically for any particular purpose or the timing of these expenditures. Accordingly, our management will have significant discretion and flexibility in applying the net proceeds from the sale of these securities. Pending their use, we intend to invest the net proceeds to us from this offering in short-term, investment-grade, interest-bearing instruments.

We believe that the net proceeds from this offering, together with our existing cash, cash equivalents and investments, will be sufficient to meet our anticipated cash requirements for a period of at least one year from the date of this prospectus.

## DIVIDEND POLICY

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all available funds and any future earnings, if any, to fund the development and expansion of our business and we do not anticipate paying any cash dividends in the foreseeable future. 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.

## CAPITALIZATION

The following table sets forth our cash, cash equivalents and investments and our capitalization as of September 30, 2019:

- on an actual basis; and
- on an as adjusted basis to give effect to the sale of 4,235,294 shares of common stock in this offering at the public offering price of \$4.25 per share, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

You should read this table together with “Selected Consolidated Financial Data,” “Management’s Discussion and Analysis of Financial Condition and Results of Operations,” “Description of Securities” and our consolidated financial statements and related notes included elsewhere in this prospectus.

	As of September 30, 2019	
	Actual	As Adjusted
	(in thousands, except share data)	
Cash, cash equivalents and investments	\$ 38,064	\$ 54,304
Long term liabilities, less current portion	\$ 5,181	\$ 5,181
Stockholders’ equity		
Class X Convertible Preferred stock, par value \$0.001 per share; 2,285,952 authorized shares; 1,643,961 shares issued and outstanding actual; 2,285,952 authorized shares; 1,643,961 shares issued and outstanding, as adjusted	2	2
Common stock, par value \$0.001 per share; 10,714,286 authorized shares, 3,890,185 shares issued and outstanding, actual; 10,714,286 authorized shares; 8,125,479 shares issued and outstanding, as adjusted	50	54
Additional paid-in capital	343,048	359,284
Accumulated other comprehensive loss	(33)	(33)
Accumulated deficit	(316,331)	(316,331)
<b>Total stockholders’ equity</b>	<b>\$ 26,736</b>	<b>\$ 42,976</b>
<b>Total capitalization</b>	<b>\$ 31,917</b>	<b>\$ 48,157</b>

If the underwriters’ exercise their over-allotment option in full, as adjusted cash, cash equivalents and investments, additional paid-in capital, total stockholders’ equity, total capitalization and shares of common stock outstanding as of September 30, 2019 would be \$56.8 million, \$361.8 million, \$45.5 million, \$50.7 million and 8,760,773 shares, respectively.

Except as otherwise indicated herein, the number of shares of our common stock to be outstanding after this offering is based on 3,890,185 shares of common stock outstanding as of September 30, 2019 and excludes:

- 389,706 shares of common stock issuable upon the exercise of stock options outstanding as of September 30, 2019, with a weighted average exercise price of \$51.35 per share;
- 12,832 shares of common stock issuable upon the vesting and settlement of restricted stock units outstanding as of September 30, 2019;
- 477,639 shares of common stock issuable upon the exercise of warrants outstanding as of September 30, 2019, with a weighted exercise price of \$64.95 per share;
- 222,014 shares of common stock reserved for future issuance under our 2015 Plan as of September 30, 2019;
- 80,299 shares of common stock reserved for future issuance under our ESPP as of September 30, 2019; and
- 587,445 shares of common stock issuable upon the conversion on 1,643,961 shares of Class X Convertible Preferred Stock outstanding as of September 30, 2019.

## DILUTION

If you invest in this offering, your ownership interest will be diluted to the extent of the difference between the public offering price per share of our common stock and the as adjusted net tangible book value per share of our common stock immediately after the closing of this offering.

Our net tangible book value as of September 30, 2019 was approximately \$26.7 million, or \$6.87 per share. Net tangible book value per share is determined by dividing our total tangible assets, less total liabilities, by the number of shares of our common stock outstanding as of September 30, 2019. Dilution with respect to net tangible book value per share represents the difference between the amount per share paid by purchasers of shares of common stock in this offering and the net tangible book value per share of our common stock immediately after this offering.

After giving effect to the sale of 4,235,294 shares of our common stock in this offering at the offering price of \$4.25 per share, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, and assuming no exercise of the underwriters' over-allotment option in full, our as adjusted net tangible book value as of September 30, 2019 would have been approximately \$43.0 million, or \$5.29 per share. This represents an immediate decrease in net tangible book value of \$1.58 per share to existing stockholders. Investors purchasing our common stock in this offering will have paid \$1.04 less than the as adjusted net tangible book value per share after this offering. The following table illustrates this on a per share basis:

Public offering price per share		\$	4.25
Net tangible book value per share as of September 30, 2019	\$	6.87	
Decrease per share attributable to new investors	\$	(1.58)	
As adjusted net tangible book value per share after this offering			5.29
Dilution in net tangible book value per share to investors purchasing shares in this offering	\$		(1.04)

If the underwriters exercise their over-allotment option in full in this offering, the as adjusted net tangible book value after the offering would be \$5.19 per share, the decrease in as adjusted net tangible book value per share to existing stockholders would be \$1.68 per share and the increase per share to new investors would be \$0.94 per share.

Except as otherwise indicated herein, the number of shares of our common stock to be outstanding after this offering is based on 3,890,185 shares of common stock outstanding as of September 30, 2019 and excludes:

- 389,706 shares of common stock issuable upon the exercise of stock options outstanding as of September 30, 2019 with a weighted average exercise price of \$51.35 per share;
- 12,832 shares of common stock issuable upon the vesting and settlement of restricted stock units outstanding as of September 30, 2019;
- 477,639 shares of common stock issuable upon the exercise of warrants outstanding as of September 30, 2019 with a weighted exercise price of \$64.95 per share;
- 222,014 shares of common stock reserved for future issuance under our 2015 Plan as of September 30, 2019;
- 80,299 shares of common stock reserved for future issuance under our ESPP as of September 30, 2019; and
- 587,445 shares of common stock issuable upon the conversion on 1,643,961 shares of Class X Convertible Preferred Stock outstanding as of September 30, 2019.

To the extent that any outstanding options or warrants are exercised, any restricted stock units vest and settle, any outstanding shares of preferred stock are converted, new options, warrants or restricted stock units are issued under our stock-based compensation plans, or new shares of preferred stock are issued, or we issue additional shares of common stock in the future, there will be further dilution to investors participating in this offering.

## SELECTED CONSOLIDATED FINANCIAL DATA

The following tables set forth our selected historical consolidated financial data as of, and for the periods ended on, the dates indicated. The selected consolidated statements of operations data for the years ended December 31, 2017 and 2018 and the selected consolidated balance sheets data as of December 31, 2017 and 2018 are derived from our audited financial statements and notes that are included elsewhere in this prospectus. The selected consolidated statements of operations data for the nine months ended September 30, 2018 and 2019 and the selected consolidated balance sheets data as of September 30, 2019 are derived from our unaudited interim consolidated financial statements and notes that are included elsewhere in this prospectus. We have prepared the unaudited consolidated financial statements in accordance with GAAP and on the same basis as the audited consolidated financial statements, except for the impact of the adoption of ASU 2016-02, *Leases*, and have included all adjustments, consisting of only normal recurring adjustments that, in our opinion, we consider necessary for a fair statement of the consolidated financial information set forth in those statements. Our historical results are not necessarily indicative of our results in any future period and results from our interim period may not necessarily be indicative of the results of the entire year.

You should read the following selected consolidated financial data together with “Management’s Discussion and Analysis of Financial Condition and Results of Operations” section and our audited and interim unaudited consolidated financial statements and the related notes included elsewhere in this prospectus. The selected audited and interim unaudited consolidated financial data in this section are not intended to replace our audited and interim unaudited consolidated financial statements and the related notes and are qualified in their entirety by the audited and interim consolidated financial statements and related notes included elsewhere in this prospectus.

	Years Ended December 31,		Nine Months Ended September 30,	
	2018	2017	2019	2018
	(in thousands, except share and per share data)		(in thousands, except share and per share data) (unaudited)	
<b>Consolidated Statements of Operations Data:</b>				
Revenues:				
Collaboration revenue	\$ —	\$ —	\$ 278	\$ —
Total revenues	—	—	278	—
Operating expenses:				
Research and development	20,385	30,067	10,458	16,836
General and administrative	12,435	17,078	6,836	10,021
Total operating expenses	32,820	47,145	17,294	26,857
Loss from operations	(32,820)	(47,145)	(17,016)	(26,857)
Total other income (expense), net	(1,695)	(1,062)	(614)	(1,336)
Net loss	\$ (34,515)	\$ (48,207)	\$ (17,630)	\$ (28,193)
Net loss per share attributable to common stock holders, basic and diluted <sup>(1)</sup>	\$ (16.11)	\$ (26.18)	\$ (5.55)	\$ (13.22)
Weighted average common stock shares outstanding, basic and diluted <sup>(1)</sup>	2,141,961	1,841,609	3,175,177	2,133,055

(1) See Note 1 to our audited and interim unaudited consolidated financial statements and related notes included elsewhere in this prospectus for a description of how we compute basic and diluted net loss per share attributable to common stockholders.

	As of December 31, 2018		As of September 30, 2019
	(in thousands)		(unaudited) (in thousands)
<b>Consolidated Balance Sheets Data:</b>			
Cash, cash equivalents and investments	\$ 49,545	\$	38,064
Working capital <sup>(1)</sup>	39,970		27,316
Total assets	52,746		43,745
Current portion of operating lease liability	—		729
Long-term operating lease liability, net of current portion	—		2,439
Current portion of long-term loans	7,767		7,844
Long-term portion of term loans, net of current portion and debt issuance costs and discount	8,263		2,742
Total stockholders' equity	33,650		26,736

(1) We define working capital as current assets less current liabilities. See our audited and interim unaudited consolidated financial statements and related notes included elsewhere in this prospectus for further details regarding our current assets and current liabilities.



## MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

*The following discussion of our financial condition and results of operations should be read together with our financial statements and related notes included elsewhere in this prospectus. This discussion contains forward-looking statements based upon our current plans, estimates, beliefs and expectations that involve risks, uncertainties and assumptions. Our actual results may differ materially from those anticipated in these forward-looking statements as a result of various factors, including those set forth under the sections entitled "Risk Factors," "Special Note Regarding Forward-Looking Statements" and elsewhere in this prospectus.*

### 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 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. 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.

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 (CSL Agreement). 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.

Since our inception in 2005, we have devoted substantially all of our resources to the therapeutic potential of tRNA synthetase biology, including the preclinical development of and clinical trials for our product candidates, the creation, licensing and protection of

related intellectual property and the provision of general and administrative support for these operations. We have not generated any revenue from product sales and, through September 30, 2019, have funded our operations primarily through the sales of equity securities and convertible debt and through venture debt and term loans.

We have never been profitable and have incurred net losses in each annual and quarterly period since our inception. For the nine months ended September 30, 2019 and 2018, we have incurred consolidated net losses of \$17.6 million and \$28.2 million, respectively. As of September 30, 2019, we had an accumulated deficit of \$316.3 million. We expect to continue to incur significant expenses and operating losses for the foreseeable future, 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. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations.

## **Financial Operations Overview**

### ***Organization and Business; Principles of Consolidation***

We conduct substantially all of our activities through aTyr Pharma, Inc., a Delaware corporation, at our facility in San Diego, California. Our condensed consolidated financial statements include our accounts and our 98% majority-owned subsidiary in Hong Kong, Pangu BioPharma Limited (Pangu BioPharma), as of September 30, 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 condensed 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 condensed 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 condensed 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 audited and interim unaudited condensed consolidated financial statements included elsewhere in this prospectus, for more information about the impact of the adoption on ASU No. 2016-02.

### ***Revenue Recognition***

We have entered into research collaborations. The terms of these arrangements may include payments to us for research and development services and potential development milestone payments.

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 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.

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

Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect that the levels of our research and development expenses will increase in the current year and will consist primarily of costs related to 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. 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 condensed consolidated financial statements, which have been prepared in accordance with generally accepted accounting principles (GAAP). The preparation of these condensed 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 condensed 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.

There have been no significant changes to our critical accounting policies since December 31, 2018, with the exception of changes made upon adoption of ASU No. 2016-02 and the related supplemental ASUs. For a description of critical accounting policies that affect our significant judgments and estimates used in the preparation of our consolidated financial statements, refer to Note 1 to our audited and interim unaudited consolidated financial statements included elsewhere in this prospectus.

## Results of Operations

### Comparison of the Three Months Ended September 30, 2019 and 2018

The following table summarizes our results of operations for the three months ended September 30, 2019 and 2018 (in thousands):

	Three Months Ended September 30,		Increase / (Decrease)
	2019	2018	
Revenues	\$ 184	\$ —	\$ 184
Research and development expenses	3,799	4,202	(403)
General and administrative expenses	1,883	2,475	(592)
Other income (expense), net	(147)	(437)	(290)

*Revenues.* Revenues consist of collaboration revenue under the CSL Agreement.

*Research and development expenses.* Research and development expenses were \$3.8 million and \$4.2 million for the three months ended September 30, 2019 and 2018, respectively. The decrease of \$0.4 million was due primarily to a decrease of \$0.6 million in costs associated with the research collaboration with The Scripps Research Institute which we terminated effective November 2018 and a decrease of \$0.2 million in non-clinical study expenses. The decrease was partially offset by an increase of \$0.4 million in expenses related to our ATYR1923 Phase 1b/2a clinical trial.

*General and administrative expenses.* General and administrative expenses were at \$1.9 million and \$2.5 million for the three months ended September 30, 2019 and 2018, respectively. The decrease of \$0.6 million was due primarily to a \$0.5 million decrease in personnel associated costs as a result of the May 2018 reduction in force, and a \$0.1 million decrease in professional fees.

*Other income (expense), net.* Other income (expense), net was \$0.1 million and \$0.4 million for the three months ended September 30, 2019 and 2018, respectively. The \$0.3 million decrease was primarily a result of lower balances on our Term Loans with the Lenders which we started paying down in June 2018.

### Comparison of the Nine Months Ended September 30, 2019 and 2018

The following table summarizes our results of operations for the nine months ended September 30, 2019 and 2018 (in thousands):

	Nine Months Ended September 30,		Increase / (Decrease)
	2019	2018	
Revenues	\$ 278	\$ —	\$ 278
Research and development expenses	\$ 10,458	\$ 16,836	(6,378)
General and administrative expenses	6,836	10,021	(3,185)
Other income (expense), net	(614)	(1,336)	(722)

*Revenues.* Revenues consist of collaboration revenue under the CSL Agreement.

*Research and development expenses.* Research and development expenses were \$10.4 million and \$16.8 million for the nine months ended September 30, 2019 and 2018, respectively. The decrease of \$6.4 million was due primarily to a \$2.7 million decrease in personnel associated costs mainly as a result of the May 2018 reduction in force, a decrease of \$1.5 million in costs associated with our research collaboration with The Scripps Research Institute which we terminated effective November 2018, a decrease of \$0.8 million related to lower product manufacturing costs, and a \$1.8 million decrease in research and development expenses which includes non-clinical studies. The decrease was offset by an increase of \$0.4 million related to our ATYR1923 Phase 1b/2a clinical trial.

*General and administrative expenses.* General and administrative expenses were at \$6.8 million and \$10.0 million for the nine months ended September 30, 2019 and 2018, respectively. The decrease of \$3.2 million was due primarily to a \$2.5 million decrease in personnel associated costs mainly as a result of the May 2018 reduction in force, and a \$0.7 million decrease in professional fees.

*Other income (expense), net.* Other income (expense), net was \$0.6 million and \$1.3 million for the nine months ended September 30, 2019 and 2018, respectively. The \$0.7 million decrease was primarily a result of lower balances on our Term Loans with the Lenders which we started paying down 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 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 September 30, 2019, we had an accumulated deficit of \$316.3 million and we expect to continue to incur net losses for the foreseeable future. As of September 30, 2019, we had cash, cash equivalents and investments of \$38.1 million. We believe that our existing cash, cash equivalents and investments will be sufficient to meet our anticipated cash requirements for a period of at least one year from the date of this prospectus.

#### 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 loan in full, subject to a prepayment fee ranging from 1.0% to 3.0% depending upon when the prepayment occurs, including any non-usage fees.

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.

#### **ATM Offering Program**

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. 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.

#### **Cash Flows**

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

	<b>Nine Months Ended September 30,</b>	
	<b>2019</b>	<b>2018</b>
Net cash (used in) provided by:		
Operating activities	\$ (15,097)	\$ (26,224)
Investing activities	6,145	39,305
Financing activities	3,331	(2,625)
Net change in cash and cash equivalents	<u>\$ (5,621)</u>	<u>\$ 10,456</u>

*Operating activities.* Net cash used in operating activities was \$15.1 million and \$26.2 million for the nine months ended September 30, 2019 and 2018, respectively. Net cash used in operating activities for the nine months ended September 30, 2019 was primarily related to our net loss of \$17.6 million, adjusted for non-cash stock-based compensation expense of \$1.4 million and net cash outflows from the changes in our operating assets and liabilities of \$0.1 million. Net cash used in operating activities for the nine months ended September 30, 2018 was primarily related to our net loss of \$28.2 million, adjusted for non-cash stock-based compensation expense of \$2.8 million and net cash outflows from the changes in our operating assets and liabilities of \$2.0 million.

*Investing activities.* Net cash used in investing activities for the nine months ended September 30, 2019 was primarily due to net maturities of investment securities of \$6.1 million. Net cash provided by investing activities for the nine months ended September 30, 2018 was primarily due to net maturities of investment securities of \$39.9 million. We invest cash in excess of our immediate operating requirements with various maturities to optimize our return on investment while satisfying our liquidity needs. Cash required for our immediate operating needs during the nine months ended September 30, 2019 was less than our immediate operating requirements during the nine months ended September 30, 2018.

*Financing activities.* Net cash provided in financing activities for the nine months ended September 30, 2019 consisted of \$4.9 million proceeds from the issuance of common stock through a registered direct offering, net of offering costs and \$4.4 million proceeds from the issuance of common stock through ATM Offering Programs, net of offering costs, offset by a \$6.0 million repayment on our Term Loans. Net cash used in financing activities for the nine months ended September 30, 2018 consisted of a \$2.7 million repayment on our Term Loans.

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>2018</b>	<b>2017</b>
<b>Net cash provided by (used in):</b>		
Operating activities	\$ (31,063)	\$ (42,364)
Investing activities	37,172	(27,637)
Financing activities	(4,238)	52,704
<b>Net increase (decrease) in cash</b>	<b>\$ 1,871</b>	<b>\$ (17,297)</b>

*Operating activities.* Net cash used in operating activities was \$31.1 million and \$42.4 million for the years ended December 31, 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, 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 in investing activities for the year ended December 31, 2018 consisted of \$37.8 million of net maturities of investment securities offset 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 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 ATM Offering Program, 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 the private placement, 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;
- 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. 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, 2018:

	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	\$ 17,083	\$ 8,000	\$ 9,083	\$ —	\$ —
Operating lease	4,310	812	2,033	1,465	—
<b>Total</b>	<b>\$ 21,393</b>	<b>\$ 8,812</b>	<b>\$ 11,116</b>	<b>\$ 1,465</b>	<b>\$ —</b>

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.

### 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 Securities and Exchange Commission (SEC).

### Emerging Growth Company Status

Under the Jumpstart Our Business Startups Act of 2012 (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.



**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).

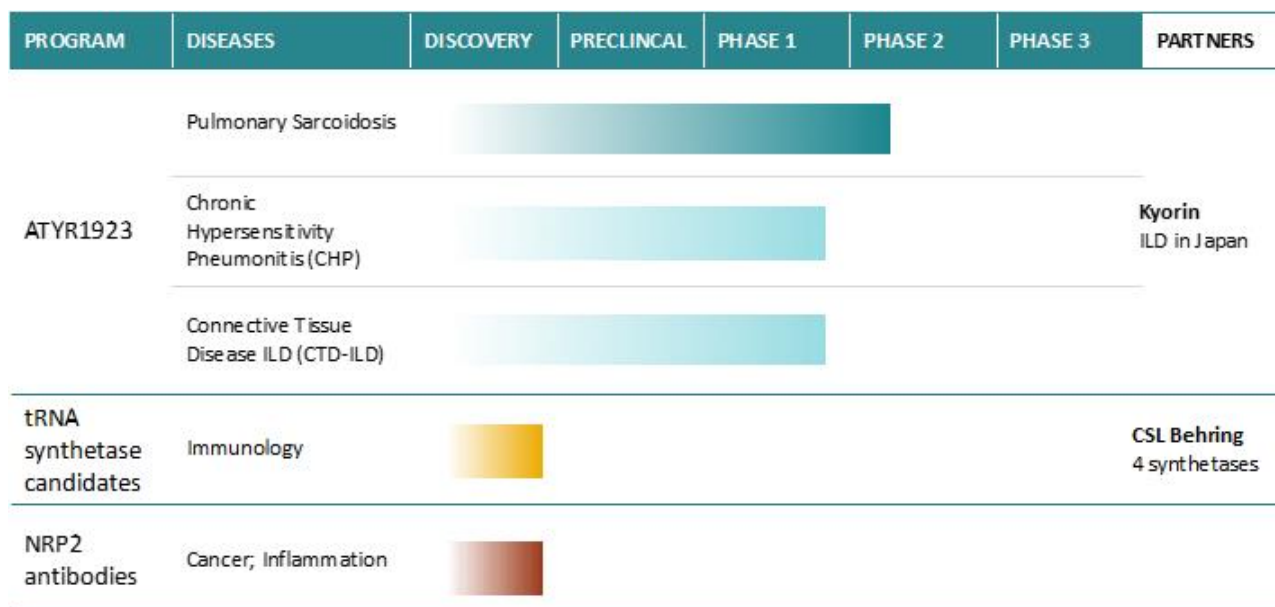
In January 2020, we entered into a license with Kyorin Pharmaceutical Co., Ltd. (Kyorin) for the development and commercialization of ATYR1923 for ILDs in Japan. Under the collaboration and license agreement with Kyorin (the Kyorin Agreement), Kyorin received an exclusive right to develop and commercialize 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.

## 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: 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.

#### Kyorin Collaboration 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.



## Hong Kong University of Science and Technology

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 collaborates 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.

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 AG, Shionogi Ltd. and Il Dong Pharmaceutical Co., Ltd., and Ofev (nintedanib), a small molecule tyrosine-kinase inhibitor marketed globally by Boehringer Ingelheim, 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, Boehringer Ingelheim, Bristol-Myers, FibroGen Inc., Galapagos NV, Gilead, Mallinckrodt and Hoffmann-La Roche 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, such as ClinicalTrials.gov.

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.

Under federal law, the fee for the submission of an NDA or BLA for which clinical data is substantial (for example, for FY2020 this application fee exceeds \$2.9 million), and the sponsor of an approved NDA or BLA is also subject to an annual program fee, currently more than \$300,000 per program. These fees are typically increased annually, but exemptions and waivers may be available under certain circumstances (such as a waiver for the first human drug application submitted by a qualifying small business and exemptions for orphan products).

The FDA has 60 days after submission of the BLA to conduct an initial review to determine whether it is sufficient to accept for filing based on the agency's threshold determination that it is sufficiently complete to permit substantive review. The FDA may request additional information rather than accept an NDA or BLA for filing. In this event, the application must be resubmitted with the additional information. The resubmitted application is also subject to review before the FDA accepts it for filing. Once the submission has been accepted for filing, the FDA begins an in-depth review of the application. Under the goals and policies under the Prescription Drug User Fee Act (PDUFA) the FDA has ten months from the filing date in which to complete its initial review of a standard application and respond to the applicant, and six months for a priority review of the application. The FDA does not always meet its PDUFA goal dates for standard and priority applications. The review process may often be significantly extended by FDA requests for additional information or clarification. The review process and the PDUFA goal date may be extended by three months if the FDA requests, or the applicant otherwise provides, additional information or clarification constituting a major amendment to the BLA submission within the last three months before the PDUFA goal date.

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. If a CRL is issued, the applicant may choose to either resubmit the NDA or BLA, addressing all of the deficiencies identified in the letter, or withdraw the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA or BLA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in response to an issued CRL in either two or six months depending on the type of information included. 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 determines the requirement for a REMS, as well as the specific REMS provisions, on a case-by-case basis. If the FDA concludes a REMS plan is needed, the sponsor of the NDA or BLA must submit a proposed REMS. The FDA will not approve a BLA without a REMS, if required. 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.

If a product receives regulatory approval from the FDA, the approval is limited to the conditions of use (e.g., patient population, indication) described in the application. Further, depending on the specific risk(s) to be addressed, the FDA may require that contraindications, warnings or precautions be included in the product labeling, require that post-approval trials, including Phase 4 clinical trials, be conducted to further assess a product's safety after approval, require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution and use restrictions or other risk management mechanisms under a REMS, which can materially affect the potential market and profitability of the product. The FDA may prevent or limit further marketing of a product based on the results of post-marketing trials or surveillance programs. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

## *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.

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.

Finally, the FDA may designate a product for priority review if it is a drug or biologic that treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines at the time that the marketing application is submitted, on a case-by-case basis, whether the proposed drug represents a significant improvement in treatment, prevention or diagnosis of disease when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting drug reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, or evidence of safety and effectiveness in a new subpopulation. A priority review designation is intended to direct overall attention and resources to the evaluation of such applications, and to shorten the FDA's goal for taking action on a marketing application from ten months to six months for an original BLA or for an NDA for a new molecular entity from the date of filing.

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. As a result, a product candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or to confirm the predicted clinical benefit of the product during post-marketing studies, would allow the FDA to withdraw approval of the drug. All promotional materials for product candidates being considered and approved under the accelerated approval program are subject to prior review by the FDA.

The accelerated approval pathway is most often used in settings in which the course of a disease is long and an extended period of time is required to measure the intended clinical benefit of a drug, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly. For example, accelerated approval has been used extensively in the development and approval of drugs for treatment of a variety of cancers in which the goal of therapy is generally to improve survival or decrease morbidity and the duration of the typical disease course requires lengthy and sometimes large clinical trials to demonstrate a clinical or survival benefit.

#### *Post-Approval Requirements*

Following approval of a new product, the manufacturer and the approved product are subject to pervasive and continuing regulation by the FDA, including, among other things, monitoring and recordkeeping activities, reporting of adverse experiences with the product, product sampling and distribution restrictions, complying with promotion and advertising requirements, which include restrictions on promoting drugs for unapproved uses or patient populations (i.e., "off-label use") and limitations on industry-sponsored scientific and educational activities. Although physicians may prescribe legally available products for off-label uses, manufacturers may not market or promote such uses. 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. If there are any modifications to the product, including changes in indications, labeling or manufacturing processes or facilities, the applicant may be required to submit and obtain FDA approval of a new NDA/BLA or an NDA/BLA supplement, which may require the applicant to develop additional data or conduct additional pre-clinical studies and clinical trials. The FDA may also place other conditions on approvals including the requirement for a REMS to assure the safe use of the product. A REMS 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. Any of these limitations on approval or marketing could restrict the commercial promotion, distribution, prescription or dispensing of products. Product approvals may be withdrawn for non-compliance with regulatory standards or if problems occur following initial marketing.

FDA regulations require that products be manufactured in specific approved facilities and in accordance with cGMPs. The cGMP regulations include requirements relating to organization of personnel, buildings and facilities, equipment, control of components and drug product containers and closures, production and process controls, packaging and labeling controls, holding and distribution, laboratory controls, records and reports and returned or salvaged products. The manufacturing facilities for our product candidates must meet cGMP requirements and satisfy the FDA, or comparable foreign regulatory authorities, before any product is approved and our commercial products can be manufactured. We rely, and expect to continue to rely, on third parties for the production of clinical and commercial quantities of our products in accordance with cGMP regulations. These manufacturers must comply with cGMP regulations



that require, among other things, quality control and quality assurance, the maintenance of records and documentation and the obligation to investigate and correct any deviations from cGMP. Manufacturers and other entities involved in the manufacture and distribution of approved drugs or biologics are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws. Accordingly, manufacturers must continue to expend time, money and effort in the area of production and quality control to maintain cGMP compliance. Future inspections by the FDA and other regulatory agencies may identify compliance issues at the facilities of our CMOs that may disrupt production or distribution or require substantial resources to correct. In addition, the discovery of conditions that violate these rules, including failure to conform to cGMPs, could result in enforcement actions, and the discovery of problems with a product after approval may result in restrictions on a product, manufacturer or holder of an approved NDA or BLA, including voluntary recall and regulatory sanctions as described below.

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

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or other enforcement-related letters or clinical holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs/BLAs or supplements to approved NDAs/BLAs, or suspension or revocation of product approvals;
- product seizure or detention, or refusal to permit the import or export of products;
- injunctions or the imposition of civil or criminal penalties; and
- consent decrees, corporate integrity agreements, debarment, or exclusion from federal health care programs; or mandated modification of promotional materials and labeling and the issuance of corrective information.

In addition, the distribution of prescription pharmaceutical products is subject to the Prescription Drug Marketing Act (PDMA) which regulates the distribution of drugs and drug samples at the federal level, and sets minimum standards for the registration and regulation of drug distributors by the states. Both the PDMA and state laws limit the distribution of prescription pharmaceutical product samples and impose requirements to ensure accountability in distribution. Most recently, the Drug Supply Chain Security Act (DSCSA) was enacted with the aim of building an electronic system to identify and trace certain prescription drugs distributed in the United States, including most biological products. The DSCSA mandates phased-in and resource-intensive obligations for pharmaceutical manufacturers, wholesale distributors, and dispensers over a 10-year period that is expected to culminate in November 2023. From time to time, new legislation and regulations may be implemented that could significantly change the statutory provisions governing the approval, manufacturing and marketing of products regulated by the FDA. It is impossible to predict whether further legislative or regulatory changes will be enacted, or FDA regulations, guidance or interpretations changed or what the impact of such changes, if any, may be.

#### *Reference product exclusivity for biological products*

In March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010 (collectively, the ACA), was enacted in the United States and included the Biologics Price Competition and Innovation Act of 2009, or the BPCIA. The BPCIA amended the PHSA to create an abbreviated approval pathway for biological products that are biosimilar to or interchangeable with an FDA-licensed reference biological product. A federal district court ruling in Texas struck down the ACA in its entirety based on constitutionality last year, and in December 2019 the Fifth Circuit Court of Appeals upheld the lower court's finding that the individual mandate imposed by the law is unconstitutional. However, the Fifth Circuit also reversed and remanded the case to the district court to determine if other reforms enacted as part of the ACA but not specifically related to the individual mandate or health insurance, including the BPCIA, could be severed from the rest of the ACA so as not to be declared invalid. It is unclear how this decision, subsequent appeals including potentially to the U.S. Supreme Court, and other efforts to repeal and replace the ACA will affect the implementation of that law and our business. To date, the FDA has approved a number of biosimilars, and numerous biosimilars have been approved in Europe. The FDA has also issued several guidance documents outlining its approach to reviewing and approving biosimilars and interchangeable biosimilars.

A biosimilar product is defined as one that is highly similar to a reference product notwithstanding minor differences in clinically inactive components and for which there are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity and potency of the product. An interchangeable product is a biosimilar product that can be expected

to produce the same clinical results as the reference product in any given patient and, for products administered multiple times to an individual, that the product and the reference product may be alternated or switched after one has been previously administered without increasing safety risks or risks of diminished efficacy relative to exclusive use of the reference biological product without such alternation or switch. Upon licensure by the FDA, an interchangeable biosimilar may be substituted for the reference product without the intervention of the health care provider who prescribed the reference product, although to date no such products have been approved for marketing in the United States.

The biosimilar applicant must demonstrate that the product is biosimilar based on data from: (1) analytical studies showing that the biosimilar product is highly similar to the reference product; (2) animal studies (including toxicity); and (3) one or more clinical studies to demonstrate safety, purity and potency in one or more appropriate conditions of use for which the reference product is approved. In addition, the applicant must show that the biosimilar and reference products have the same mechanism of action for the conditions of use on the label, route of administration, dosage and strength, and the production facility must meet standards designed to assure product safety, purity and potency.

A reference biological product is granted 12 years of data exclusivity from the time of first licensure of the product, and the first approved interchangeable biologic product will be granted an exclusivity period of up to one year after it is first commercially marketed. If pediatric studies are performed and accepted by the FDA as responsive to a written request, the 12-year exclusivity period will be extended for an additional six months. In addition, the FDA will not accept an application for a biosimilar or interchangeable product based on the reference biological product until four years after the date of first licensure of the reference product. "First licensure" typically means the initial date the particular product at issue was licensed in the United States. Date of first licensure does not include the date of licensure of (and a new period of exclusivity is not available for) a supplement for the reference product for a subsequent application filed by the same sponsor or manufacturer of the reference product (or licensor, predecessor in interest or other related entity) for a change (not including a modification to the structure of the biological product) that results in a new indication, route of administration, dosing schedule, dosage form, delivery system, delivery device or strength or for a modification to the structure of the biological product that does not result in a change in safety, purity or potency. Therefore, one must determine whether a new product includes a modification to the structure of a previously licensed product that results in a change in safety, purity or potency to assess whether the licensure of the new product is a first licensure that triggers its own period of exclusivity. Whether a subsequent application, if approved, warrants exclusivity as the "first licensure" of a biological product is determined on a case-by-case basis with data submitted by the sponsor.

The BPCIA is complex and only beginning to be interpreted and implemented by the FDA. In addition, recent government proposals have sought to reduce the 12-year reference product exclusivity period. Other aspects of the BPCIA, some of which may impact the BPCIA exclusivity provisions, have also been the subject of recent litigation. As a result, the ultimate impact, implementation and meaning of the BPCIA is subject to significant uncertainty.

#### *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. Importantly, United States authorities that enforce the FCPA, including the Department of Justice, deem most health care professionals and other employees of foreign hospitals, clinics, research facilities and medical schools in countries with public health care or public education systems to be “foreign officials” under the FCPA. When we interact with foreign health care professionals and researchers in testing and marketing our products abroad, we must have policies and procedures in place sufficient to prevent us and agents acting on our behalf from providing any bribe, gift or gratuity, including excessive or lavish meals, travel or entertainment in connection with marketing our products and services or securing required permits and approvals such as those needed to initiate clinical trials in foreign jurisdictions. The FCPA also obligates companies whose securities are listed in the United States to comply with accounting provisions requiring the maintenance of books and records that accurately and fairly reflect all transactions of the corporation, including international subsidiaries, and the development and maintenance of an adequate system of internal accounting controls for international 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.

#### *Health care reform in the United States and potential changes to health care laws*

The FDA’s and other regulatory authorities’ policies may change and additional government regulations may be enacted that could prevent, limit or delay regulatory approval of our product candidates. For example, in December 2016, the 21st Century Cures Act (Cures Act) was signed into law. The Cures Act, among other things, is intended to modernize the regulation of drugs and devices and to spur innovation, but its ultimate implementation is uncertain. In addition, in August 2017, the FDA Reauthorization Act was signed into law, which reauthorized the FDA’s user fee programs and included additional drug and device provisions that build on the Cures Act. If we are slow or unable to adapt to changes in existing requirements or the adoption of new requirements or policies, or if we are not able to maintain regulatory compliance, we may lose any marketing approval that we otherwise may have obtained and we may not achieve or sustain profitability, which would adversely affect our business, prospects, financial condition and results of operations.

As previously mentioned, a primary trend in the United States health care industry and elsewhere is cost containment. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medical products and services, implementing reductions in Medicare and other health care funding and applying new payment methodologies. For example, in March 2010, the ACA was enacted, which, among other things, increased the minimum Medicaid rebates owed by most manufacturers under the Medicaid Drug Rebate Program; introduced a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected; extended the Medicaid Drug Rebate Program to utilization of prescriptions of individuals enrolled in Medicaid managed care plans; imposed mandatory discounts for certain Medicare Part D beneficiaries as a condition for manufacturers’ outpatient drugs coverage under Medicare Part D; and established a Center for Medicare Innovation at the United States Centers for Medicare and Medicaid Services (CMS) to test innovative payment and service delivery models to lower Medicare and Medicaid spending.

Since its enactment, there have been judicial and Congressional challenges to certain aspects of the ACA, and we expect there will be additional challenges and amendments to the ACA in the future. The current Presidential administration and members of the United States Congress have indicated that they may continue to seek to modify, repeal or otherwise invalidate all, or certain provisions of, the ACA. For example, the Tax Cuts and Jobs Acts was enacted in 2017, which, among other things, removed penalties for not complying with the individual mandate to carry health insurance. As noted above, a 2018 federal district court ruling struck down the ACA in its entirety although the Fifth Circuit Court of Appeals recently limited it to the individual mandate and remanded the case to the district court to determine if other reforms not specifically related to the individual mandate or health insurance could be severed from the rest of the ACA. It is unclear how this decision, subsequent appeals including potentially to the U.S. Supreme Court, and other efforts to repeal and replace the ACA will affect the implementation of that law and our business.

In addition, other legislative changes have been proposed and adopted in the United States since the ACA that affect health care expenditures. There has been heightened governmental scrutiny in recent years over the manner in which manufacturers set prices for their marketed products, which has resulted in several 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 pharmaceutical and biologic products. Notably, on

December 20, 2019, President Trump signed the Further Consolidated Appropriations Act for 2020 into law (P.L. 116-94) that includes a piece of bipartisan legislation called the Creating and Restoring Equal Access to Equivalent Samples Act of 2019 (CREATES Act). The CREATES Act aims to address the concern articulated by both the FDA and others in the industry that some brand manufacturers have improperly restricted the distribution of their products, including by invoking the existence of a REMS for certain products, to deny generic and biosimilar product developers access to samples of brand products. Because generic and biosimilar product developers need samples to conduct certain comparative testing required by the FDA, some have attributed the inability to timely obtain samples as a cause of delay in the entry of generic and biosimilar products. To remedy this concern, the CREATES Act establishes a private cause of action that permits a generic or biosimilar product developer to sue the brand manufacturer to compel it to furnish the necessary samples on “commercially reasonable, market-based terms.” Whether and how generic and biosimilar product developments will use this new pathway, as well as the likely outcome of any legal challenges to provisions of the CREATES Act, remain highly uncertain and its potential effects on our future commercial products are unknown.

We cannot predict the likelihood, nature or extent of government regulation that may arise from future legislation or administrative or executive action, either in the United States or abroad. We expect that additional state and federal health care reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for health care products and services.

### **Employees**

As of January 10, 2020, 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 audited and interim unaudited consolidated financial statements included elsewhere in this prospectus.

### **Facilities**

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.

### **Legal Proceedings**

From time to time, we may become involved in various claims and legal proceedings. We are not currently a party to any legal proceedings that, in the opinion of our management, are likely to have a material adverse effect on our business. Regardless of outcome, litigation can have an adverse impact on us because of defense and settlement costs, diversion of management resources and other factors.

## MANAGEMENT

### Executive Officers and Directors

The following table sets forth certain information about our executive officers and directors as of January 10, 2020:

Name	Age	Position
<i>Executive Officers</i>		
Sanjay S. Shukla, M.D., M.S.	48	President, Chief Executive Officer and Director
Jill M. Broadfoot	58	Chief Financial Officer
Nancy E. Denyes	52	General Counsel and Corporate Secretary
<i>Non-Employee Directors</i>		
John K. Clarke (1)(2)(3)	66	Chairman of the Board
James C. Blair, Ph.D. (2)(3)	80	Director
Timothy P. Coughlin (1)(2)	53	Director
Jane A. Gross, Ph.D.	62	Director
Jeffrey S. Hatfield (1)(3)	61	Director
Svetlana Lucas, Ph.D.	48	Director
Paul Schimmel, Ph.D.	79	Director

(1) Member of the Audit Committee.

(2) Member of the Compensation Committee.

(3) Member of the Nominating and Corporate Governance Committee.

### Executive Officers

**Sanjay S. Shukla, M.D., M.S.** has served as our President and Chief Executive Officer and as a director since November 2017. Dr. Shukla served as our Chief Medical Officer from March 2016 to November 2017. From April 2015 to March 2016, Dr. Shukla worked in an advisory capacity for a number of companies, including as a consultant to our company from January 2016 to March 2016. Prior to that, from October 2012 to April 2015, Dr. Shukla served as Vice President and Global Head of Integrated Medical Services for Novartis, a biopharmaceutical company, where he led global medical affairs operations, with oversight for all pharma general medicines therapies, both inline and in development. Dr. Shukla served as Chief Executive Officer of RXMD, a clinical development consultancy that assisted in advancing proof of concept for early stage drug candidates, from April 2009 to September 2012. Prior to that, Dr. Shukla served in a variety of clinical development, data analytics and drug safety roles at Vifor Pharma, a biopharmaceutical company, and Aspreva Pharmaceuticals (acquired by Vifor Pharma). Dr. Shukla received his M.D. from Howard University College of Medicine and his Bachelors of Science in microbiology and Master of Science in epidemiology and biostatistics from the University of Maryland. Our Board of Directors believes that Dr. Shukla is qualified to serve on our Board of Directors due to his experience as our Chief Executive Officer and previously as our Chief Medical Officer, as well as his medical background, experience in the life science industry and his leadership experience.

**Jill M. Broadfoot** has served as our Chief Financial Officer since July 2018. From January 2017 to July 2018, Ms. Broadfoot served as Chief Financial Officer of Emerald Health Pharmaceuticals Inc. and Emerald Health Bioceticals Inc., where she was responsible for establishing operations for the U.S.-based pharmaceutical and biocetrical entities as well as the establishment of operations, corporate governance, finance and accounting and investor relations functions, among others. Prior to Emerald Health, Ms. Broadfoot served as Vice President, U.S. Corporate Controller at GW Pharmaceuticals, from May 2016 to January 2017. While at GW Pharmaceuticals, her responsibilities included establishing U.S. commercial operations and implementing U.S. public company financial and accounting standards in connection with the transfer of corporate operations from the U.K. to the U.S. Prior to joining GW Pharmaceuticals, Ms. Broadfoot served as Chief Financial Officer of Vical Inc., from October 2004 to March 2013, where she had oversight of finance, investor relations, manufacturing, information technology, human resources, and business development. Prior to that, Ms. Broadfoot held various positions at DJO Global, Inc., most recently as Vice President of Finance, and served as an audit manager at Ernst & Young LLP. Ms. Broadfoot holds a B.S. in business administration and accounting from San Diego State University and is a Certified Public Accountant.

**Nancy E. Denyes** has served as our General Counsel since February 2019 and as our Corporate Secretary since January 2015. Ms. Denyes served as our Vice President, Legal Affairs from October 2014 to February 2019, and provided consulting services to us from 2013 to 2014. Ms. Denyes practiced law in the corporate department at Cooley LLP and was named partner in 2000. Her practice at Cooley was focused on securities and corporate matters, including private financings, public offerings, mergers and acquisitions and corporate governance and disclosure issues. Ms. Denyes holds a J.D. from the University of California, Berkeley School of Law and a B.A. in economics and business from the University of California, Los Angeles.



## **Non-Employee Directors**

**John K. Clarke** has served as Chairman of our Board of Directors since September 2005. Mr. Clarke is Managing Partner of Cardinal Partners, a venture capital firm focused on healthcare investing. He co-founded Cardinal Partners in 1997 and has served as President of CHP Management, Inc. since that time. He currently serves as a director on the boards of various privately held biotechnology companies including Abide Therapeutics, Inc., Vividion Therapeutics, Inc. and Ivenix Corporation. He has also served as a director for several biotechnology and biopharmaceutical companies including Alnylam Pharmaceuticals, Inc., Momenta Pharmaceuticals, Inc., Verastem, Inc. and Sirtis Pharmaceuticals, Inc. (acquired by GlaxoSmithKline); healthcare information technology companies, including TechRx Technology Services Corporation (acquired by NDCHealth) and Visicu, Inc. (acquired by Phillips Electronics); and a privately held biopharmaceutical company, Rib-X Pharmaceuticals Inc. Mr. Clarke holds an A.B. in economics and biology from Harvard University and an M.B.A. from the Wharton School at the University of Pennsylvania. Our Board of Directors believes Mr. Clarke is qualified to serve on our Board of Directors due to his extensive experience within the field of drug discovery and development and his broad leadership experience on various public and private company boards.

**James C. Blair, Ph.D.** has served as a director since December 2010. Dr. Blair has been a Partner of Domain Associates, a venture capital firm with a focus on life sciences, since the company's founding in 1985. Present Board memberships include Clovis Oncology, Inc., a biopharmaceutical company, as well as numerous private company boards. Dr. Blair currently serves on the Board of Directors of the Prostate Cancer Foundation and the Sanford Burnham Prebys Medical Discovery Institute. He is also on the advisory board of the Department of Molecular Biology at Princeton University. Dr. Blair holds a B.S.E. in electrical engineering from Princeton University and an M.S.E. and Ph.D. in electrical engineering from the University of Pennsylvania. Our Board of Directors believes that Dr. Blair is qualified to serve on our Board of Directors due to his experience in the life science industry and his years of business and leadership experience.

**Timothy P. Coughlin** has served as a director since April 2017. Mr. Coughlin is the former Chief Financial Officer of Neurocrine Biosciences, Inc. Neurocrine, a biopharmaceutical company that has received FDA approval for INGREZZA (valbenazine) and ORILISSA (elagolix), both of which were discovered and developed during his tenure at Neurocrine from 2002 to 2018. Prior to joining Neurocrine, he was with Catholic Health Initiatives, a nationwide integrated healthcare delivery system, where he served as Vice President, Financial Services. Mr. Coughlin also served as a Senior Manager in the Health Sciences practice of Ernst & Young LLP and its predecessors from 1989 to 1999. Mr. Coughlin serves on the Board of Directors of Retrophin, Inc. and Fate Therapeutics, Inc., both biotechnology companies. He also served on the Board of Directors of Peloton Therapeutics prior to its sale to Merck & Co in 2019. Mr. Coughlin holds a master's degree in international business from San Diego State University and a bachelor's degree in accounting from Temple University. Mr. Coughlin is a certified public accountant in both California and Pennsylvania. Our Board of Directors believes that Mr. Coughlin is qualified to serve on our Board of Directors due to his extensive background in financial and accounting matters for public companies, his experience in the life science industry and his years of business and leadership experience.

**Jane A. Gross, Ph.D.** has served as a director since June 2019. Dr. Gross currently serves as Chief Scientific Officer, Senior Vice President, Research and Development of Aptevo Therapeutics Inc. (Aptevo), a position she has held since September 2016. In this role, Dr. Gross led the discovery of novel protein therapeutics based on the ADAPTIR platform in immuno-oncology, leading research efforts in molecular biology and protein engineering, immunology, protein and cell sciences, pharmacology and translational research. Prior to joining Aptevo, Dr. Gross served as Vice President, Applied Research and Non-Clinical Development at Emergent BioSolutions Inc. and Vice President, Immunology Research at ZymoGenetics, Inc., where she led efforts in discovery and development of therapeutics from novel genes. Dr. Gross holds a Ph.D. in Immunology from the University of California, Berkeley under Jim Allison (2018 recipient of the Nobel Prize in Physiology and Medicine) and a Post-Doctoral Fellowship from the University of Washington in Immunology. Our Board of Directors believes that Dr. Gross is qualified to serve on our Board of Directors due to her extensive experience in the biotherapeutics industry and her expertise in immunology and oncology.

**Jeffrey S. Hatfield** has served as a director since April 2017. Mr. Hatfield currently serves as Chief Executive Officer and a member of the Board of Directors at Zafgen, a biopharmaceutical company dedicated to significantly improving the health and well-being of patients affected by metabolic diseases. Previously, Mr. Hatfield served as President, Chief Executive Officer and a member of the Board of Directors of Vitae Pharmaceuticals from 2004 to 2016. As CEO, Mr. Hatfield successfully transitioned Vitae from a novel platform technology start-up to a thriving product-focused company with a robust pipeline of multiple first-in-class clinical stage and pre-clinical stage assets generated from the company's internal discovery engine. Mr. Hatfield took the company public in 2014, and in October 2016, Vitae Pharmaceuticals was acquired by Allergan plc for approximately \$639.0 million in cash. Prior to joining Vitae Pharmaceuticals, Mr. Hatfield worked at Bristol-Myers Squibb in a variety of executive positions, including: Senior Vice President of BMS's Immunology and Virology Divisions, where he was responsible for all aspects of the \$1.0 billion business; President and General Manager, Canada; and, Vice President, U.S. Managed Health Care. He previously served as a Board member of Ambit Biosciences before its acquisition by Daiichi-Sankyo in 2015, and as a member of the Board of Directors of the Biotechnology Industry Organization (BIO), serving on the Executive Company Section. Mr. Hatfield currently serves as Chairman of the Board of Miragen Therapeutics, a biotherapeutic company, and as an Adjunct Professor and member of the Dean's Advisory Committee for Purdue

University's College of Pharmacy, where he is a Distinguished Alumnus. Mr. Hatfield holds an M.B.A. from The Wharton School, University of Pennsylvania and a bachelor's degree in pharmacy from Purdue University. Our Board of Directors believes Mr. Hatfield is qualified to serve on our Board of Directors due to his extensive experience within the field of drug discovery and development and his broad leadership experience.

**Svetlana Lucas, Ph.D.** has served as a director since June 2019. Dr. Lucas currently serves as a Chief Business Officer at Scribe Therapeutics, a private biotechnology company. Prior to her current role, she served as Senior Vice President, Business Development at Tizona Therapeutics, Inc. (Tizona), a clinical stage immunotherapy company, where she was responsible for the company's business development strategy and transactions, including global strategic collaboration with AbbVie Inc (AbbVie). Before joining Tizona, Dr. Lucas was Head of Oncology and Inflammation External R&D at Amgen Inc. (Amgen), where she oversaw business development activities, including Amgen's strategic cancer immunotherapy research collaboration and licensing agreement with Kite Pharma, and collaborated with Amgen Ventures on several investments in oncology and inflammation. Dr. Lucas joined Amgen following the acquisition of Onyx Pharmaceuticals, Inc. (Onyx), where she spearheaded the company's oncology partnering strategy and due diligence of new opportunities. Prior to Onyx, she held positions of increasing responsibility in strategy, business development and strategic marketing at Amgen, PDL BioPharma/Facet Biotech (acquired by AbbVie), and XOMA Corporation. She began her career as a strategy consultant in the Life Sciences practice of McKinsey & Company, Inc. Dr. Lucas received her Ph.D. in Molecular Biology and Biochemistry from California Institute of Technology, and an undergraduate degree in Biology from Moscow State University. Our Board of Directors believes that Dr. Lucas is qualified to serve on our Board of Directors due to her extensive business development experience in the biotherapeutics industry.

**Paul Schimmel, Ph.D.** has served as a director since September 2005. Dr. Schimmel is currently a director of Alnylam Pharmaceuticals, Inc., a biopharmaceutical company, as well as a director of several private companies. He was a cofounder of Repligen Corporation, Alkermes, Inc. Cubist Pharmaceuticals, Sirtris Pharmaceuticals, and Alnylam Pharmaceuticals, and a founding Director of Momenta, Inc. Dr. Schimmel is an Ernest and Jean Hahn Professor of Molecular Medicine and of Chemistry at Scripps Research. He was formerly the John D. and Catherine T. MacArthur Professor of Biochemistry and Biophysics in the Department of Biology at the Massachusetts Institute of Technology. Dr. Schimmel holds a B.A. from Ohio Wesleyan University and a Ph.D. in biochemistry and biophysics from the Massachusetts Institute of Technology. He is an elected member of the National Academy of Sciences, the National Academy of Medicine, the National Academy of Inventors, the American Philosophical Society and the American Academy of Arts and Sciences. Our Board of Directors believes Dr. Schimmel is qualified to serve on our Board of Directors due to his role as one of our scientific founders and his discoveries and scientific leadership in the field of tRNA synthetase biology and other areas important to the development of therapeutics.

Our executive officers are elected by, and serve at the discretion of, our Board of Directors. There are no family relationships among any of our directors and executive officers.

#### **Composition of our Board of Directors**

Our amended and restated certificate of incorporation provides for a Board of Directors that is divided into three classes. The term for each class is three years, staggered over time. Our Board of Directors is currently comprised of eight members. The next election of Class II directors will be at our 2020 annual meeting of stockholders, with the elected candidate(s) to then serve until our 2023 annual meeting of stockholders. The directors in Class II are Dr. James C. Blair, Mr. Timothy P. Coughlin and Dr. Jane A. Gross. The next election of Class III directors will be at our 2021 annual meeting of stockholders, with the elected candidate(s) to then serve until our 2024 annual meeting of stockholders. The directors in Class III are Mr. Jeffrey S. Hatfield and Dr. Sanjay S. Shukla and Dr. Svetlana Lucas. The next election of Class I directors will be at our 2022 annual meeting of stockholders, with the elected candidate(s) to then serve until our 2025 annual meeting of stockholders. The directors in Class I are Mr. John K. Clarke and Dr. Paul Schimmel.

Our Board of Directors has determined that all of our directors, except for Dr. Shukla, are independent, as determined in accordance with the rules of the Nasdaq Stock Market (Nasdaq) and the SEC. In addition, Dr. Mendlein, who resigned from our Board of Directors on June 28, 2019, was not determined to be independent. In making such independence determination, the Board of Directors considered the relationships that each non-employee director has with us and all other facts and circumstances that the Board of Directors deemed relevant in determining their independence, including the beneficial ownership of our capital stock by each non-employee director. In considering the independence of the directors listed above, our Board of Directors considered the association of our directors with the holders of more than 5% of our common stock.

#### **Role of the Board of Directors in Risk Management**

Risk is inherent with every business, and how well a business manages risk can ultimately determine its success. We face a number of risks, including risks relating to our financial condition, development and commercialization activities, operations and intellectual property. Management is responsible for the day-to-day management of risks we face, while our Board of Directors, as a whole and through its committees, has responsibility for the oversight of risk management. In its risk oversight role, our Board of

Directors has the responsibility to satisfy itself that the risk management processes designed and implemented by management are adequate and functioning as designed.

The role of our Board of Directors in overseeing the management of our risks is conducted primarily through committees of the Board of Directors, as disclosed in the descriptions of each of the committees below and in the charters of each of the committees. The full Board of Directors (or the appropriate board committee in the case of risks that are under the purview of a particular committee) discusses with management our major risk exposures, their potential impact on our company, and the steps we take to manage them. When a board committee is responsible for evaluating and overseeing the management of a particular risk or risks, the chairman of the relevant committee reports on the discussion to the full Board of Directors during the committee reports portion of the next board meeting. This enables our Board of Directors and its committees to coordinate the risk oversight role, particularly with respect to risk interrelationships.

### **Committees of the Board of Directors**

Our Board of Directors has a standing Audit Committee, Compensation Committee and Nominating and Corporate Governance Committee. Each of our Audit Committee, Compensation Committee and Nominating and Corporate Governance Committee is composed entirely of independent directors in accordance with current Nasdaq listing standards. Furthermore, our Audit Committee meets the enhanced independence standards established by the Sarbanes-Oxley Act and related rulemaking of the SEC.

#### ***Audit Committee***

Mr. Clarke, Mr. Coughlin and Mr. Hatfield currently serve on the Audit Committee, which is chaired by Mr. Coughlin. Our Board of Directors has designated Mr. Coughlin as an “Audit Committee financial expert,” as defined under the applicable rules of the SEC. The Audit Committee’s responsibilities include:

- appointing, approving the compensation of, and assessing the independence of our independent registered public accounting firm;
- approving auditing and permissible non-audit services, and the terms of such services, to be provided by our independent registered public accounting firm;
- reviewing the internal audit plan with the independent registered public accounting firm and members of management responsible for preparing our financial statements;
- reviewing and discussing with management and the independent registered public accounting firm our annual and quarterly financial statements and related disclosures as well as critical accounting policies and practices used by us;
- reviewing the adequacy of our internal control over financial reporting;
- establishing policies and procedures for the receipt and retention of accounting-related complaints and concerns;
- recommending, based upon the Audit Committee’s review and discussions with management and the independent registered public accounting firm, whether our audited financial statements shall be included in our Annual Report on Form 10-K;
- monitoring the integrity of our financial statements and our compliance with legal and regulatory requirements as they relate to our financial statements and accounting matters;
- preparing the Audit Committee report required by SEC rules to be included in our annual proxy statement;
- reviewing all related party transactions for potential conflict of interest situations and approving all such transactions; and
- reviewing quarterly earnings releases.

We believe that the composition and functioning of our Audit Committee complies with all applicable requirements of the Sarbanes-Oxley Act, and all applicable SEC and Nasdaq rules and regulations. We intend to comply with future requirements to the extent they become applicable to us.

#### ***Compensation Committee***

Dr. Blair, Mr. Clarke and Mr. Coughlin currently serve on the Compensation Committee, which is chaired by Dr. Blair. The Compensation Committee’s responsibilities include:

- annually reviewing and approving corporate goals and objectives relevant to the compensation of our Chief Executive Officer;
- evaluating the performance of our Chief Executive Officer in light of such corporate goals and objectives and recommending the compensation of our Chief Executive Officer to the Board of Directors for approval;
- reviewing and approving the compensation of our other officers;
- reviewing and establishing our overall management and employee compensation, philosophy and policy;
- overseeing and administering our compensation and similar plans;
- evaluating and assessing potential and current compensation advisors in accordance with the independence standards identified in the applicable Nasdaq Stock Market and SEC rules;
- retaining and approving the compensation of any compensation advisors;
- reviewing and approving our policies and procedures for the grant of equity-based awards;
- reviewing and making recommendations to our Board of Directors with respect to director compensation;
- preparing the compensation committee report required by the SEC rules to be included in our annual proxy statement;
- reviewing and discussing with management the compensation discussion and analysis to be included in our annual proxy statement or Annual Report on Form 10-K; and
- reviewing and discussing with our Board of Directors corporate succession plans for the Chief Executive Officer and other key officers.

We believe that the composition and functioning of our Compensation Committee complies with all applicable requirements of the Sarbanes-Oxley Act, and all applicable SEC and Nasdaq rules and regulations. We intend to comply with future requirements to the extent they become applicable to us.

#### ***Nominating and Corporate Governance Committee***

Dr. Blair, Mr. Clarke and Mr. Hatfield currently serve on the Nominating and Corporate Governance Committee, which is chaired by Mr. Clarke. The Nominating and Corporate Governance Committee's responsibilities include:

- developing and recommending to the Board of Directors criteria for board and committee membership;
- establishing procedures for identifying and evaluating Board of Director candidates, including nominees recommended by stockholders;
- identifying individuals qualified to become members of the Board of Directors;
- recommending to the Board of Directors the persons to be nominated for election as directors and to each of the Board's committees;
- developing and recommending to the Board of Directors a set of corporate governance guidelines; and
- overseeing the evaluation of the Board of Directors.

We believe that the composition and functioning of our Nominating and Corporate Governance Committee complies with all applicable requirements of the Sarbanes-Oxley Act, and all applicable SEC and Nasdaq rules and regulations. We intend to comply with future requirements to the extent they become applicable to us.

## EXECUTIVE AND DIRECTOR COMPENSATION

### COMPENSATION OF DIRECTORS

In April 2015, our Board of Directors adopted a non-employee director compensation policy, which became effective upon the completion of our initial public offering in May 2015, that is designed to provide a total compensation package that enables us to attract and retain, on a long-term basis, high-caliber non-employee directors. In January 2016 and February 2017, our Board of Directors adopted amendments to the policy with respect to the cash and equity component of compensation to our non-employee directors. Under this policy, as amended to date, all non-employee directors are paid cash compensation for service on the Board of Directors and committees of the Board of Directors as set forth below, prorated based on days of service during a calendar year.

Board of Directors	Annual Retainer
All non-employee members	\$ 37,500
Additional retainer for Chairperson	\$ 35,000
<b>Audit Committee:</b>	
Chairperson	\$ 25,000
Non-Chairperson members	\$ 8,000
<b>Compensation Committee:</b>	
Chairperson	\$ 10,000
Non-Chairperson members	\$ 5,000
<b>Nominating and Corporate Governance Committee:</b>	
Chairperson	\$ 7,500
Non-Chairperson members	\$ 4,000

In addition, under the policy, each new non-employee director who is initially appointed or elected to our Board of Directors will receive an option grant to purchase up to 2,285 shares of common stock, which will vest in equal monthly installments during the 36 months following the grant date, subject to the director's continued service on our Board of Directors. Thereafter, on the date of each annual meeting of stockholders, each continuing non-employee director will be eligible to receive an annual option grant to purchase up to 1,428 shares of common stock, which will vest in full upon the earlier of the first anniversary of the date of grant or the date of the following annual meeting of stockholders, subject to the director's continued service on our Board of Directors. All of the foregoing options will be granted with an exercise price equal to the fair market value of our common stock on the date of grant.

We have agreed to reimburse all reasonable out-of-pocket expenses incurred by non-employee directors in attending Board and committee meetings.

#### Director Compensation Table—2019

The following table sets forth information with respect to the compensation earned by our non-employee directors during the fiscal year ended December 31, 2019. During 2019, Dr. Shukla did not receive compensation for his service on the Board of Directors. The compensation paid to Dr. Shukla as an employee of our company is set forth under the heading "Compensation of Executive Officers—Summary Compensation Table" below.

Name	Fees Earned or Paid in Cash	Option Awards <sup>(1)</sup>	Total
John K. Clarke (Chairman) <sup>(2)</sup>	\$ 93,000	\$ 8,936	\$ 101,936
James C. Blair, Ph.D. <sup>(3)</sup>	\$ 51,500	\$ 8,936	\$ 60,436
Timothy P. Coughlin <sup>(4)</sup>	\$ 67,500	\$ 8,936	\$ 76,436
Jane A. Gross, Ph.D. <sup>(5)</sup>	\$ 19,059	\$ 9,216	\$ 28,275
Jeffrey S. Hatfield <sup>(6)</sup>	\$ 37,500	\$ 8,936	\$ 46,436
Svetlana Lucas, Ph.D. <sup>(7)</sup>	\$ 19,059	\$ 9,216	\$ 28,275
John D. Mendlein, Ph.D. <sup>(8)</sup>	\$ 18,750	\$ —	\$ 18,750
Amir H. Nashat, Sc.D. <sup>(9)</sup>	\$ 16,125	\$ —	\$ 16,125
Paul Schimmel, Ph.D. <sup>(10)</sup>	\$ 37,500	\$ 8,936	\$ 46,436

(1) In accordance with SEC rules, this column reflects the aggregate grant date fair value of the option awards granted during 2019 computed in accordance with FASB Topic 718. These amounts do not reflect the actual economic value that may be realized by the directors upon the vesting of the stock options, the exercise of the stock options or the sale of the common stock underlying such stock options. Our non-employee directors will only realize compensation to the extent the trading price of our common stock is greater than the exercise price of such stock options.

(2) Mr. Clarke held stock options to purchase an aggregate of 7,405 shares of common stock as of December 31, 2019.

(3) Dr. Blair held stock options to purchase an aggregate of 7,405 shares of common stock as of December 31, 2019.

- (4) Mr. Coughlin held stock options to purchase an aggregate of 6,569 shares of common stock as of December 31, 2019.
- (5) Dr. Gross held stock options to purchase an aggregate of 2,285 shares of common stock as of December 31, 2019.
- (6) Mr. Hatfield held stock options to purchase an aggregate of 6,569 shares of common stock as of December 31, 2019.
- (7) Dr. Lucas held stock options to purchase an aggregate of 2,285 shares of common stock as of December 31, 2019.
- (8) Dr. Mendlein resigned from our Board of Directors effective as of June 28, 2019. During 2019, Dr. Mendlein also received fees of \$90,000 pursuant to a Strategic Advisor Agreement. Dr. Mendlein held stock options to purchase an aggregate of 38,053 shares of common stock as of December 31, 2019.
- (9) Dr. Nashat completed his service on our Board of Directors as of our 2019 Annual Meeting of Stockholders on May 8, 2019 and therefore has not served on our Board of Directors since that date and did not receive the annual option grant on May 8, 2019. Dr. Nashat held stock options to purchase an aggregate of 6,875 shares of common stock as of December 31, 2019.
- (10) Dr. Schimmel held stock options to purchase an aggregate of 7,907 shares of common as of December 31, 2019.

## COMPENSATION OF EXECUTIVE OFFICERS

The following table presents information regarding the total compensation earned by each individual who served as our chief executive officer at any time during the fiscal year ended December 31, 2019, and our two other most highly compensated executive officers who were serving as executive officers as of December 31, 2019. We refer to these officers in this prospectus as our named executive officers. The following table also sets forth information regarding total compensation earned by each of our named executive officers during the fiscal year ending December 31, 2019 and 2018.

### SUMMARY COMPENSATION TABLE

The following table presents all of the compensation awarded to or earned by or paid to our named executive officers during the fiscal years indicated below.

Name and Principal Position	Year	Salary (\$)	Stocks Awards (\$) <sup>(1)</sup>	Option Awards (\$) <sup>(1)</sup>	Non-Equity Incentive Plan Compensation (\$) <sup>(2)</sup>	All Other Compensation (\$) <sup>(3)</sup>	Total (\$)
Sanjay S. Shukla, M.D., M.S. <i>President and Chief Executive Officer</i>	2019	450,000	25,860	82,400		10,076	568,336
	2018	450,000	—	780,000	140,549	9,916	1,380,465
Jill M. Broadfoot <sup>(4)</sup> <i>Chief Financial Officer</i>	2019	350,000	12,930	20,600		11,594	395,124
	2018	148,526	—	121,880	58,324	5,393	334,123
Nancy E. Denyes <sup>(5)</sup> <i>General Counsel</i>	2019	335,000	—	51,500		12,932	399,432

(1) Amounts shown reflect aggregate full grant date fair value of equity-based awards granted during the year in accordance with FASB ASC Topic 718. Pursuant to FASB ASC Topic 718, the amounts shown exclude the impact of estimated forfeitures related to service-based vesting conditions.

(2) The amounts reported for 2018 reflect the cash bonus determined by our Compensation Committee (for the named executive officers other than Dr. Shukla), and by our Board of Directors upon recommendation of our Compensation Committee (for Dr. Shukla), based on certain performance goals and achievement of certain developmental, clinical or regulatory milestones as specified by our Board of Directors upon recommendation of our Compensation Committee. The amount of bonus earned by each of our named executive officers in 2019 is not calculable and accordingly has not been determined. The amount of bonus, if any, for each of our named executive officers is expected to be determined by February 2020, at which time we will disclose the amount of bonus, if any, for each of our named executive officers.

(3) The amounts reported in 2019 in this column include: (i) 401(k) employer match of \$9,500 and life insurance premium of \$576 to Dr. Shukla; (ii) 401(k) employer match of \$11,018 and life insurance premium of \$576 to Ms. Broadfoot; and (iii) HSA employee contribution of \$3,900, 401(k) employer match of \$8,456 and life insurance premium of \$576 to Ms. Denyes.

(4) Ms. Broadfoot joined our company and was appointed as our Chief Financial Officer on July 30, 2018.

(5) Ms. Denyes was promoted to General Counsel on February 6, 2019 and did not serve as an executive officer in 2018.

**Base Salaries.** Our Compensation Committee reviews the base salaries of our executive officers, including our named executive officers, from time to time and makes adjustments as it determines to be reasonable and necessary to reflect the scope of an executive officer's performance, contributions, responsibilities, experience, prior salary level, position (in the case of a promotion) and market conditions.

**Bonuses.** In January 2016, the Board of Directors adopted our Senior Executive Cash Incentive Bonus Plan (Bonus Plan), which applies to certain key executives (Executives), that are recommended by the Compensation Committee and selected by the Board of Directors. The Bonus Plan provides for bonus payments based upon the attainment of performance targets established by the Compensation Committee and related to operational and financial metrics with respect to our company or any of our subsidiaries (Performance Goals), which may include achievement of specified research and development, publication, clinical and/or regulatory milestones, total shareholder return, earnings before interest, taxes, depreciation and amortization, net income (loss) (either before or after interest, taxes, depreciation, stock compensation expense, restructuring charges and/or amortization), changes in the market price of our common stock, economic value-added, funds from operations or similar measure, sales or revenue, acquisitions or strategic transactions, operating income (loss), cash flow (including, but not limited to, operating cash flow and free cash flow), return on capital, assets, equity, or investment, return on sales, gross or net profit levels, productivity, expense, margins, operating efficiency, customer satisfaction, working capital, earnings (loss) per share of our common stock, sales or market shares and number of customers. Any bonuses paid under the Bonus Plan will be based upon objectively determinable bonus formulas that tie such bonuses to one or more performance targets relating to the Performance Goals. The bonus formulas will be adopted in each performance period by the Compensation Committee and communicated to each Executive. No bonuses will be paid under the Bonus Plan unless and until the Compensation Committee makes a determination with respect to the attainment of the performance objectives. Notwithstanding the foregoing, the Compensation Committee may adjust bonuses payable under the Bonus Plan based on achievement of individual

performance goals or pay bonuses (including, without limitation, discretionary bonuses) to Executives under the Bonus Plan based upon such other terms and conditions as the Compensation Committee may in its discretion determine.

*Equity Incentive Compensation.* We generally grant stock options to our employees, including our named executive officers, in connection with their initial employment with us. We also have historically granted stock options on an annual basis as part of annual performance reviews of our employees.

### Outstanding Equity Awards at Fiscal Year-End

The following table sets forth certain information with respect to outstanding equity awards held by each of our named executive officers as of December 31, 2019:

Name	Vesting Commencement Date	Option Awards					Stock Awards		
		Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable	Equity Incentive Plan Awards: Number of Securities Underlying Unexercised Unearned Options (#)	Option Exercise Price (\$)	Option Expiration Date	Number of shares of stock that have vested (#)	Number of shares of stock that have not vested (#)	Market value of shares of stock that have not vested (\$)
Sanjay S. Shukla, M.D., M.S.	3/30/2016	10,914 (1)	728 (1)	—	68.04	3/30/2026			
	9/13/2016	1,596 (2)	368 (2)	—	42.84	9/13/2026			
	2/7/2017	3,288 (2)	1,354 (2)	—	46.20	2/7/2027			
	11/1/2017	16,741 (2)	15,401 (2)	—	56.00	11/1/2027			
	2/6/2018	9,821 (2)	11,607 (2)	—	46.20	2/6/2028			
	2/6/2019	2,976 (2)	11,309 (2)	—	7.24	2/6/2029			
	2/6/2019	—	—	—	—	—	—	3,571 (3)	14,891
Jill M. Broadfoot	7/30/2018	5,060 (1)	9,225 (1)	—	11.41	7/30/2028			
	2/6/2019	744 (2)	2,827 (2)	—	7.24	2/6/2029			
	2/6/2019	—	—	—	—	—	—	1,785 (3)	7,443
Nancy E. Denyes	10/10/2014	2,542 (1)	—	—	248.36	10/10/2024			
	4/17/2015	448 (2)	—	—	128.10	4/17/2025			
	5/6/2015	628 (2)	—	—	196	5/6/2025			
	10/1/2015	1,214 (2)	—	—	143.36	10/1/2025			
	1/27/2016	1,398 (2)	30 (2)	—	85.96	1/27/2026			
	9/13/2016	2,119 (2)	488 (2)	—	42.84	9/13/2026			
	2/7/2017	1,771 (2)	729 (2)	—	46.20	2/7/2027			
	2/6/2018	1,637 (2)	1,934 (2)	—	46.20	2/6/2028			
	5/16/2018	1,885 (2)	1,686 (2)	—	11.90	5/16/2028			
	5/16/2018	—	—	—	—	—	893	892 (3)	3,720
2/6/2019	1,860	7,068	—	7.24	2/6/2029				

- (1) 1/4th of the shares subject to the option vest one year from Vesting Commencement Date and the remaining shares subject to the option vest in 36 equal monthly installments following the one-year anniversary of the Vesting Commencement Date. The option is subject to full acceleration in the event the employee is terminated by our company without Cause or resigns for Good Reason within the period commencing two months prior to and ending 12 months following a Change in Control or Sale Event (as such capitalized terms are defined in the 2015 Plan, as applicable or the respective stock option agreements evidencing such stock option).
- (2) 1/48th of the total shares subject to the option vest monthly from the Vesting Commencement Date set forth in the table above. The option is subject to full acceleration in the event the employee is terminated by our company without Cause or resigns for Good Reason within the period commencing two months prior to and ending 12 months following a Change in Control or Sale Event (as such capitalized terms are defined in the 2015 Plan, as applicable or the respective stock option agreements evidencing such stock option).
- (3) Vests in two equal annual installments from Vesting Commencement Date set forth in the table above. The award is subject to accelerated vesting upon termination without cause upon a Change of Control.



*401(k) Savings Plan and Other Benefits.* We maintain a tax-qualified retirement plan (401(k) Plan), that provides eligible U.S. employees with an opportunity to save for retirement on a tax advantaged basis. Eligible employees are able to defer eligible compensation subject to applicable annual Code limits. Employees' pre-tax contributions are allocated to each participant's individual account and are then invested in selected investment alternatives according to the participants' directions. Employees are immediately and fully vested in their contributions. Our 401(k) Plan is intended to be qualified under Section 401(a) of the Code with our 401(k) Plan's related trust intended to be tax exempt under Section 501(a) of the Code. As a tax-qualified retirement plan, contributions to our 401(k) Plan and earnings on those contributions are not taxable to the employees until distributed from our 401(k) Plan. We match employee contributions under the 401(k) Plan in an amount up to 3% of each applicable employee's compensation (equivalent to a 50% match with respect to up to 6% of such employee's compensation). We also pay, on behalf of our employees, a significant portion of premiums for health, life and disability insurance.

#### **Employment Arrangements with Our Named Executive Officers**

We consider it essential to the best interests of our stockholders to attract high quality executives and foster the continuous employment of our key management personnel. In this regard, we believe some severance arrangements are necessary. We also recognize that the possibility of a change in control may exist and that the uncertainty and questions that it may raise among management could result in the departure or distraction of management personnel to the detriment of our company and our stockholders. In order to reinforce and encourage the continued attention and dedication of certain key members of management, on December 21, 2015, the Compensation Committee approved the Executive Severance and Change in Control Policy (Policy). The purpose of the Policy is to provide certain of our senior management employees with compensation and benefits in the event of a termination of employment without Cause or for Good Reason (as such terms are defined in the Policy).

The post-termination compensation and benefits under the Policy include the (i) acceleration of time-based vesting provisions of outstanding equity awards that would have vested within 12 months of the termination, (ii) severance in the amount of 12 months of base salary, and (iii) payment of the employer portion of group health care benefits under COBRA for up to 12 months after termination.

In addition, if the termination occurs within two months prior to or one year after the closing of a Sale Event (as defined in the Policy), then, in lieu of the benefits described above, such eligible employee is entitled to (i) full acceleration of time-based vesting provisions of all outstanding equity awards, (ii) severance in the amount of 12 months of base salary, (iii) payment of the employee's bonus target for the calendar year in which the termination occurred, and (iv) payment of the employer portion of group health care benefits under COBRA for up to 12 months after termination.

In each case, receipt of any compensation or benefits under the Policy is subject to the eligible employee's execution of a severance agreement and release.

To the extent Section 280G of the Code is applicable with respect to payments to an eligible employee, such eligible employee shall be entitled to receive either: (a) payment of the full amounts set forth above to which the eligible employee is entitled or (b) payment of such lesser amount that does not trigger excise taxes under Section 4999 of the Code, whichever results in the employee receiving a higher amount after taking into account all federal, state, and local income, excise and employment taxes.

Employees who are party to an agreement or an arrangement with us that provides greater benefits in the aggregate than set forth in the Policy are not eligible to receive any payments or benefits under the Policy.

In addition, we have also entered into a written employment agreement with our President and Chief Executive Officer that provides for payments in connection with the resignation, retirement or other termination of such named executive officer, or a change in control, as described below.

#### ***Sanjay S. Shukla, M.D., M.S.***

Dr. Shukla entered into an at-will employment offer letter with us on March 30, 2016 to serve as our Chief Medical Officer, which provided for an initial base salary of \$375,000, subject to adjustments as determined by us in our sole discretion. Pursuant to the terms of his employment offer letter, Dr. Shukla was considered annually for a bonus target, in an amount of up to 40% of his then-current base salary, as determined by our Board of Directors based on corporate achievements of goals and achievement of Dr. Shukla's individual goals.

On November 1, 2017, we announced a leadership transition whereby Dr. Shukla, our then-current Chief Medical Officer, succeeded Dr. Mendlein, our then-current Chief Executive Officer, as our President, Chief Executive Officer, and principal executive officer effective as of November 1, 2017 (CEO Transition).

Under the terms of an employment agreement with Dr. Shukla entered November 1, 2017 (CEO Employment Agreement), Dr. Shukla is entitled to an initial annual base salary of \$450,000, subject to annual review and increase as determined by the Compensation Committee. In addition, Dr. Shukla is eligible for an annual bonus target, in the amount of 45% of his then-current base salary for the rest of 2017, and then in an amount of 50% of his then-current base salary for subsequent calendar years, as determined by the Compensation Committee. Dr. Shukla was granted an option to purchase 32,142 shares of our common stock, effective as of November 1, 2017, pursuant to the 2015 Plan.

Dr. Shukla's employment is at-will. In the event that Dr. Shukla's employment is terminated by Dr. Shukla for Good Reason or by us without Cause (as such terms are defined below), Dr. Shukla will be entitled to receive (i) the amount of his accrued but unpaid salary and unpaid expense reimbursements and any accrued but unused vacation as of the date of termination, (ii) any vested benefits Dr. Shukla may have under any employee benefit plan, which shall be paid in accordance with the terms of such employee benefit plans, as of the date of termination, (iii) any earned but unpaid incentive compensation from the prior calendar year, (iv) an amount equal to Dr. Shukla's current annual base salary plus his annual target incentive compensation in the year of termination, (v) acceleration of the time-based vesting provisions of all stock options or other stock-based awards that would have vested within 12 months of the termination, and (vi) payment of the amount that would reasonably be required to obtain equivalent health insurance coverage for up to 12 months after termination, in the case of each of (iv), (v) and (vi), subject to the execution of a separation agreement and release.

In the event that Dr. Shukla's employment is terminated by us without Cause or by Dr. Shukla for Good Reason within two months prior and 12 months after any Change in Control, as such terms are defined below, Dr. Shukla is entitled to (i) a cash payment equal to his then-current base salary plus his annual target incentive compensation in the year of termination, (ii) full acceleration of the time-based vesting provisions of all outstanding stock options or other stock-based awards, and (iii) payment of the amount that would reasonably be required to obtain equivalent health insurance coverage for up to 12 months after termination.

Under the CEO Employment Agreement, the terms below are generally defined as follows:

"Cause" means (i) conduct by the employee constituting a material act of willful misconduct in connection with the performance of his duties; (ii) the employee's conviction of, or the entry of a pleading of guilty or nolo contendere by the employee to, any crime involving (A) fraud or embezzlement in either case that results in material damage to us or any of our subsidiaries or affiliates or (B) any felony; (iii) willful and repeated failure by the employee to substantially perform the duties, functions and responsibilities of his positions that result in material damage to us or any of our subsidiaries and affiliates, that continues after he has received prior written notice from the Board of Directors of such purported repeated failure, which notice details the grounds of such purported repeated failure and requests its cure, and the employee has been given a reasonable opportunity to cure which will not be less than 30 days; or (iv) a material breach by the employee of any of the material provisions contained in the CEO Employment Agreement which has continued for more than 30 days following written notice of such purported breach; and

"Change in Control" means (i) any "person", as such term is used in Sections 13(d) and 14(d) of the Exchange Act (other than our company, any of our subsidiaries, or any trustee, fiduciary or other person or entity holding securities under any employee benefit plan or trust of our company or any of our subsidiaries), together with all "affiliates" and "associates" (as such terms are defined in Rule 12b-2 under the Exchange Act) of such person, shall become the "beneficial owner" (as such term is defined in Rule 13d-3 under the Exchange Act), directly or indirectly, of securities of our company representing 50 percent or more of the combined voting power of our then outstanding securities having the right to vote in an election of the Board (Voting Securities) (in such case other than as a result of an acquisition of securities directly from us); (ii) the date a majority of the members of the Board of Directors is replaced during any 12-month period by directors whose appointment or election is not endorsed by a majority of the members of the Board of Directors before the date of the appointment or election; or (iii) the consummation of (A) any consolidation or merger of our company or any subsidiary of our company where the stockholders of our company, immediately prior to the consolidation or merger, would not, immediately after the consolidation or merger, beneficially own (as such term is defined in Rule 13d-3 under the Exchange Act), directly or indirectly, shares representing in the aggregate more than 50 percent of the voting shares of our company issuing cash or securities in the consolidation or merger (or of its ultimate parent corporation, if any), or (B) any sale or other transfer (in one transaction or a series of transactions contemplated or arranged by any party as a single plan) of all or substantially all of the assets of our company; provided, however, that with respect to clause (A) above and as approved by the Board of Directors, a Change of Control shall be deemed to have occurred upon the consummation of a transaction whereby shares representing in the aggregate of more than 30 percent but less than 50 percent of the voting shares of our company are beneficially owned by the acquiring party or parties and such transaction includes a contingent right for the acquiring party or parties to acquire additional voting shares of our company that would represent more than 50 percent of our company's voting shares in the aggregate.

“Good Reason” means (i) a material diminution in the Executive’s responsibilities, authority or duties; (ii) a material diminution in the Executive’s Base Salary except for across-the-board salary reductions based on our company’s financial performance similarly affecting all or substantially all senior management employees of our company; or (iii) relocation of our executive headquarters to a location more than 50 miles from San Diego, California.

***Jill M. Broadfoot***

Ms. Broadfoot entered into an at-will employment offer letter with us on July 16, 2018, which provided for an initial base salary of \$350,000, subject to adjustments as determined by us in our sole discretion. Pursuant to the terms of her employment offer letter, Ms. Broadfoot is eligible for an annual bonus, currently in a target amount of up to 40% of her then-current base salary, as determined by our Board of Directors based on corporate achievements of goals and achievement of Ms. Broadfoot’s individual goals.

Ms. Broadfoot is also eligible to receive certain post-termination compensation and benefits in accordance with the Policy described above.

***Nancy E. Denyes***

Ms. Denyes entered into an at-will employment offer letter with us on October 7, 2014, which provided for an initial base salary of \$240,000, subject to adjustments as determined by us in our sole discretion.

Ms. Denyes is also eligible to receive certain post-termination compensation and benefits in accordance with the Policy described above.

**CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS**

Other than the compensation agreements and other arrangements described under “Compensation of Executive Officers” and the transactions described below, since January 1, 2017, there has not been and there is not currently proposed, any transaction or series of similar transactions to which we were, or will be, a party in which the amount involved exceeded, or will exceed, \$120,000 or 1% of the average of our total assets at year end for the last two completed fiscal years, and in which any director, executive officer, holder of five percent or more of any class of our capital stock or any member of the immediate family of, or entities affiliated with, any of the foregoing persons, had, or will have, a direct or indirect material interest.

**Payments to The Scripps Research Institute**

We provided funding to The Scripps Research Institute (TSRI) under an amended and restated research funding and option agreement, as amended (the Research Funding and Option Agreement). In May 2018, we terminated the Research Funding and Option Agreement, effective as of November 10, 2018. From January 1, 2017 to November 10, 2018, we paid \$3.4 million to TSRI under the Research Funding and Option Agreement. Paul Schimmel, Ph.D., one of our directors, is a faculty member at TSRI and such payments funded a portion of his research activities conducted at TSRI.

**Executive Officer and Director Compensation**

***Employment Agreements***

We have entered into offer letters or employment agreements with each of our named executive officers. For more information regarding these arrangements, see Executive and Director Compensation.

***Stock Option Awards***

For information regarding stock option awards and other equity incentive awards granted to our named executive officers and directors, see “Executive and Director Compensation.”

***John D. Mendlein, Ph.D. – Strategic Advisor Agreement***

Dr. Mendlein served as a strategic advisor to us pursuant to the terms of an advisor agreement entered with Dr. Mendlein in November 2017 (the Strategic Advisor Agreement). In June 2019, Dr. Mendlein resigned from our Board of Directors and, in August 2019, we gave notice to terminate the Strategic Advisor Agreement effective September 2019. Pursuant to the terms of the Strategic Advisor Agreement, we agreed to: (i) pay Dr. Mendlein as a strategic advisor to us for a period of up to four years, at a monthly rate of \$42,500 for the first year and \$7,500 per month for the rest of the term (which amount totaled \$600,000); (ii) as part of our annual review of compensation, pay Dr. Mendlein a to-be-determined cash bonus in February 2018 with respect to 2017 performance (which amount totaled \$165,750); (iii) reimburse Dr. Mendlein for certain benefits continuation through December 31, 2018 (which amount totaled \$19,256); (iv) allow for continued vesting of Dr. Mendlein’s outstanding time-based employee stock options for so long as Dr. Mendlein

provided services to our company as a strategic advisor; and (v) provide for an extended option exercise period with respect to certain employee stock options held by Dr. Mendlein.

### **Participation in this Offering**

Paul Schimmel, Ph.D., a stockholder and member of our Board of Directors, has indicated an interest in purchasing up to a number of shares of the common stock offered in this offering as would maintain his current pro-rata percentage ownership of our common stock. Because indications of interest are not binding agreements or commitments to purchase, he may determine to purchase fewer or more shares than he has indicated an interest in purchasing, or elect not to purchase any shares in this offering. The underwriters may also determine to sell fewer, more or no shares in this offering to him.

### **Indemnification Agreements**

We have entered into agreements to indemnify our directors and executive officers. These agreements will, among other things, require us to indemnify these individuals for certain expenses (including attorneys' fees), judgments, fines and settlement amounts reasonably incurred by such person in any action or proceeding, including any action by or in our right, on account of any services undertaken by such person on behalf of our company or that person's status as a member of our Board of Directors to the maximum extent allowed under Delaware law.

### **Procedures for Approval of Related Person Transactions**

The Audit Committee conducts an appropriate review of all related person transactions for potential conflict of interest situations on an ongoing basis, and the approval of the Audit Committee is required for all such transactions. The Audit Committee follows the policies and procedures set forth in our written Related Person Transaction Policy in order to facilitate such review.

## PRINCIPAL STOCKHOLDERS

The following table sets forth the beneficial ownership of our common stock as of January 10, 2020 by: (i) each of the executive officers named in the table under the heading “Summary Compensation Table,” (ii) each current director, (iii) all current directors and executive officers as a group, and (iv) all persons known to us to be the beneficial owners of more than 5% of our common stock. The table is based upon information supplied by our executive officers, directors and principal stockholders and a review of filings by the beneficial owners with the SEC pursuant to Sections 13(d) and 13(g) of the Exchange Act.

We have determined beneficial ownership in accordance with the rules and regulations of the SEC, and the information is not necessarily indicative of beneficial ownership for any other purpose. In computing the number of shares beneficially owned by a person and the percentage ownership of such person, we deemed to be outstanding all shares subject to options held by the person that are currently exercisable or exercisable as of March 10, 2020, which is 60 days after January 10, 2020. These shares are deemed to be outstanding and beneficially owned by the person holding such options for the purpose of computing the percentage ownership of that person, but they are not treated as outstanding for the purpose of computing the percentage ownership of any other person. Except as indicated by the footnotes below, we believe, based on information furnished to us, that the persons and entities named in the table below have sole voting and sole investment power with respect to all shares that they beneficially own, subject to applicable community property laws.

Applicable percentage ownership before the offering is based on 4,300,034 shares of our common stock outstanding as of January 10, 2020. Applicable percentage ownership after the offering is based on 8,535,328 shares of common stock outstanding immediately after the closing of this offering.

Paul Schimmel, Ph.D., a stockholder and member of our Board of Directors, has indicated an interest in purchasing up to a number of shares of the common stock offered in this offering as would maintain his current pro-rata percentage ownership of our common stock. Because indications of interest are not binding agreements or commitments to purchase, he may determine to purchase fewer or more shares than he has indicated an interest in purchasing, or elect not to purchase any shares in this offering. The underwriters may also determine to sell fewer, more or no shares in this offering to him. The following table does not reflect any potential purchase by Dr. Schimmel, which purchase, if any, will increase the percentage of shares owned after the offering from that set forth in the table below.

<u>Beneficial Owner(1)</u>	<u>Number of Shares of Common Stock Owned (2)</u>	<u>Number of Shares of Common Stock Acquirable Within 60 Days (3)</u>	<u>Total Number of Shares of Common Stock Beneficially Owned (4)</u>	<u>Percentage of Shares Beneficially Owned Before the Offering</u>	<u>Percentage of Shares Beneficially Owned After the Offering</u>
<b>5% Stockholders:</b>					
Federated Investors Inc. (5) 1001 Liberty Avenue Pittsburgh, PA 15222	550,000	—	550,000	12.8%	6.4 %
FMR LLC (6) 245 Summer Street, Boston, Massachusetts 02210	491,449	—	491,449	11.4%	5.8 %
Viking Global Investors LP (7) 55 Railroad Avenue, Greenwich, Connecticut 06830	408,247	—	408,247	9.5%	4.8 %
<b>Directors and Named Executive Officers:</b>					
Sanjay S. Shukla, M.D., M.S. (8)	250	52,220	52,470	1.2%	* %
Jill M. Broadfoot (9)	6,607	7,515	14,122	*	* %
Nancy E. Denyes (10)	1,987	16,775	18,762	*	* %
John K. Clarke (11)	133,075	5,977	139,052	3.2%	1.6 %
James C. Blair, Ph.D. (12)	130,988	5,977	136,965	3.2%	1.6 %
Timothy P. Coughlin (13)	—	5,078	5,078	*	* %
Jane A. Gross, Ph.D. (14)	—	508	508	*	* %
Jeffrey S. Hatfield (15)	—	5,078	5,078	*	* %
Svetlana Lucas, Ph.D. (16)	—	508	508	*	* %
Paul Schimmel, Ph.D. (17)	249,500	6,479	255,979	5.9%	3.0 %
All directors and executive officers as a group (10 persons) (18)	522,407	106,115	628,522	14.3%	4.0 %

\* Represents beneficial ownership of less than 1% of the shares of common stock.

(1) Unless otherwise indicated, the address for each beneficial owner is c/o aTyr Pharma, Inc., 3545 John Hopkins Court, Suite #250, San Diego, CA 92121.

(2) Represents shares of common stock owned, excluding shares of common stock that are listed under the heading "Number of Shares of Common Stock Acquirable Within 60 Days," by the named parties as of January 10, 2020.

(3) Shares of common stock subject to stock options, restricted stock units, warrants or Preferred Shares acquirable within 60 days of January 10, 2020, regardless of exercise price, are deemed to be outstanding for computing the percentage ownership of the person holding such options and the percentage ownership of any group of which the holder is a member, but are not deemed outstanding for computing the percentage of any other person.

(4) Beneficial ownership is determined in accordance with the rules of the SEC and generally includes voting or investment power with respect to securities. Except as indicated by footnote, and subject to community property laws where applicable, we believe that the persons named in the table have sole voting and investment power with respect to all shares of common stock shown as beneficially owned by them.

(5) Based on Schedule 13F filed with the SEC on November 14, 2019. Federated Investors, Inc. (the Parent) is the parent holding company of Federated Equity Management Company of Pennsylvania and Federated Global Investment Management Corp. (the Investment Advisers), which act as investment advisers to registered investment companies and separate accounts that own shares of common stock in us (the Reported Securities). The Investment Advisers are wholly owned subsidiaries of FII Holdings, Inc., which is a wholly owned subsidiary of Federated Investors, Inc., the Parent. All of the Parent's outstanding voting stock is held in the Voting Shares Irrevocable Trust (the Trust) for which Thomas R. Donahue, Rhodora J. Donahue and J. Christopher Donahue act as trustees (collectively, the Trustees). The Parent, the Trust, and each of the Trustees expressly disclaim beneficial ownership of the Reported Securities in which they do not have an actual pecuniary interest.

(6) Based on Schedule 13F filed with the SEC on November 13, 2019, which indicates that FMR LLC had sole voting power with respect to 48,188 shares of common stock and had sole power to dispose or to direct the disposition of 491,449 shares of common stock. Abigail P. Johnson is a Director, the Chairman and the Chief Executive Officer of FMR LLC. Members of the Johnson family including Abigail P. Johnson, are the predominant owners, directly or through trusts, of Series B voting common shares of FMR LLC, representing 49% of the voting power of FMR LLC. The Johnson family group and all other Series B shareholders have entered into a shareholders' voting agreement under which all Series B voting common shares will be voted in accordance with the majority vote of Series B voting common shares. Accordingly, through their ownership of voting common shares and the execution of the shareholders' voting agreement, members of the Johnson family may be deemed, under the Investment Company Act of 1940, to form a controlling group with respect to FMR LLC. Neither FMR LLC nor Abigail P. Johnson have the sole power to vote or direct the voting of the shares owned directly by the various investment companies registered under the Investment Company Act (Fidelity Funds) advised by Fidelity Management & Research Company (FMR Co), a wholly owned subsidiary of FMR LLC, which power resides with the Fidelity Funds' Boards of Trustees. Fidelity Management & Research Company carries out the voting of the shares under written guidelines established by the Fidelity Funds' Boards of Trustees.

(7) Based on Notice of Conversion letter from Viking Global Opportunities Portfolio GP LLC dated January 7, 2020.

(8) Includes (i) 250 shares of common stock held by Dr. Shukla; and (ii) 52,220 shares of common stock that Dr. Shukla has the right to acquire from us within 60 days of January 10, 2020 pursuant to the exercise of stock options or vesting of restricted stock units.

- (9) Includes (i) 6,607 shares of common stock held by Ms. Broadfoot; and (ii) 7,515 shares of common stock that Ms. Broadfoot has the right to acquire from us within 60 days January 10, 2020 pursuant to the exercise of stock options or vesting of restricted stock units.
- (10) Includes (i) 1,987 shares of common stock held by Ms. Denyes; and (ii) 16,775 shares of common stock that Ms. Denyes has the right to acquire from us within 60 days January 10, 2020 pursuant to the exercise of stock options.
- (11) Includes (i) 7,492 shares of common stock held by our director, Mr. Clarke; and (ii) 5,977 shares of common stock that Mr. Clarke has the right to acquire from us within 60 days of January 10, 2020 pursuant to the exercise of stock options. Based on Schedule 13G filed with the SEC on February 4, 2016, which indicates that 125,583 shares of common stock are held by CHP II, L.P. (CHP). The general partner of CHP is CHP II Management, LLC (CHP Management), which may be deemed to beneficially own certain of the shares held by CHP. CHP Management disclaims beneficial ownership of all shares held by CHP in which it does not have an actual pecuniary interest. John Clarke, Brandon Hull and John Park are managing members of CHP Management and as members of the general partner, they may be deemed to beneficially own certain of the shares held by CHP Management. The managing members disclaim beneficial ownership of all shares held by CHP Management in which they do not have an actual pecuniary interest.
- (12) Includes (i) 449 shares of common stock held by our director, Dr. Blair; and (ii) 5,977 shares of common stock that Dr. Blair has the right to acquire from us within 60 days of January 10, 2020 pursuant to the exercise of stock options. Based on Schedule 13G filed with the SEC on January 19, 2016, consists of (i) 129,130 shares held by Domain Partners VIII, L.P.; (ii) 959 shares held by DP VIII Associates, L.P.; and (iii) 450 shares held by Domain Associates, LLC. Each of the funds has sole voting and dispositive power over such shares. One Palmer Square Associates VIII, LLC (One Palmer) is the general partner of Domain Partners and Domain Associates and may be deemed to have sole voting and investment power over such shares. One Palmer disclaims beneficial ownership of all shares held by Domain Partners and Domain Associates in which it does not have an actual pecuniary interest. Dr. Blair, is a managing member of One Palmer. Dr. Blair disclaims beneficial ownership of all shares held by One Palmer in which he does not have an actual pecuniary interest.
- (13) Represents 5,078 shares of common stock that Mr. Coughlin has the right to acquire from us within 60 days of January 10, 2020 pursuant to the exercise of stock options.
- (14) Represents 508 shares of common stock that Dr. Gross has the right to acquire from us within 60 days of January 10, 2020 pursuant to the exercise of stock options.
- (15) Represents 5,078 shares of common stock that Mr. Hatfield has the right to acquire from us within 60 days of January 10, 2020 pursuant to the exercise of stock options.
- (16) Represents 508 shares of common stock that Dr. Lucas has the right to acquire from us within 60 days of January 10, 2020 pursuant to the exercise of stock options.
- (17) Includes (i) 2,889 shares of common stock held by our director, Dr. Schimmel; (ii) 63,022 shares of common stock held by the Paul Schimmel Prototype PSP, Paul Schimmel, Trustee, FBO Paul Schimmel (Prototype PSP); (iii) 183,589 shares of common stock held by the Schimmel Revocable Trust U/A Dtd 9/6/2000; and (iv) 6,479 shares of common stock that Dr. Schimmel has the right to acquire from us within 60 days of January 10, 2020 pursuant to the exercise of stock options.
- (18) Includes the number of shares beneficially owned by the named executive officers and directors listed in the above table.

## DESCRIPTION OF SECURITIES

The following description summarizes some of the terms of our amended and restated certificate of incorporation and amended and restated bylaws and of the Delaware General Corporation Law. The following description does not purport to be complete and is subject to, and qualified in its entirety by, our amended and restated certificate of incorporation and bylaws, which are exhibits to the registration statement of which this prospectus forms a part.

### Authorized Capital Stock

As of September 30, 2019, our authorized capital stock consists of 10,714,286 shares of common stock, par value \$0.001 per share, and 7,285,456 shares of preferred stock, par value \$0.001 per share, of which 72,000 shares are designated Series B redeemable convertible preferred stock, 15,957 shares are designated Series C redeemable convertible preferred stock, 2,197,499 shares are designated Series D redeemable convertible preferred stock, 2,285,952 shares are designated Class X Convertible Preferred Stock and 2,714,048 shares are undesignated preferred stock. The designated preferred stock is not available for future issuance. As of September 30, 2019, we had 3,890,185 shares of common stock outstanding and 1,643,961 shares of Class X Convertible Preferred Stock outstanding. As of September 30, 2019, there were 40 stockholders of record of our common stock.

### 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. All outstanding shares are fully paid and nonassessable.

### 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.

### Preferred Stock

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. As a result of the designation and issuance of 2,285,952 shares of Class X Convertible Preferred Stock described below, our Board of Directors is authorized to designate and issue up to 2,714,048 remaining shares of preferred stock. 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 our preferred stock could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive dividend payments and payments upon our liquidation. In addition, the issuance of preferred stock could have the effect of delaying, deferring or preventing a change in control of our company or other corporate action.

We filed a Certificate of Designation of Preferences, Rights and Limitations of Class X Convertible Preferred Stock with the Secretary of State of Delaware on August 28, 2017 (Certificate of Designation), pursuant to which we designated 2,285,952 shares of authorized and unissued preferred stock as Class X Convertible Preferred Stock (Preferred Shares). Each Preferred Share is convertible into five shares of common stock (subject to adjustment for stock dividends, stock splits, combinations and the like). The current holder of the Preferred Shares will be prohibited from converting their Preferred Shares into shares of common stock if, as a result of such conversion, such holder, together with any other persons whose beneficial ownership of our common stock would be aggregated with such holder's for purposes of Section 13(d) and Section 16 of the Exchange Act and the applicable regulations of the SEC, would beneficially own more than 9.50% of the shares of our common stock then issued and outstanding, which percentage may change at such holder's election upon 61 days' notice to us. Additionally, in the event of certain fundamental transactions, including (i) any merger or consolidation of our company with or into another individual or corporation, partnership, trust, incorporated or unincorporated



association, joint venture, limited liability company, joint stock company, government (or an agency or subdivision thereof) or other entity of any kind, in which our company is not the survivor or the stockholders of our company immediately prior to such merger or consolidation do not own, directly or indirectly, at least 50% of the voting securities of the surviving entity, (ii) any sale of all or substantially all of its assets or a majority of its common stock is acquired by a third party, in each case, in one or a series of related transactions, (iii) any tender offer or exchange offer (whether by our company or another person) is completed pursuant to which all or substantially all of the holders of common stock are permitted to tender or exchange their shares for other securities, cash or property, or (iv) any reclassification of the common stock or any compulsory share exchange pursuant to which the common stock is effectively converted into or exchanged for other securities, cash or property (other than as a result of certain subdivisions or combinations of shares of common stock), each share of Class X Convertible Preferred Stock outstanding immediately prior to such fundamental transaction will automatically convert into shares of common stock at the applicable conversion ratio.

In the event of our liquidation, dissolution or winding up, holders of Preferred Shares will participate *pari passu* with the holders of our common stock in any distribution of proceeds, pro rata based on the number of shares held by each such holder on an as-converted basis. The Preferred Shares have no voting rights. Holders of the Preferred Shares are entitled to receive, on an as-converted-to-common-stock basis, dividends that are equal to dividends actually paid on shares of common stock, when, as and if such dividends are paid on shares of the common stock.

The purpose of authorizing our Board of Directors to issue preferred stock in one or more series and determine the number of shares in the series and its rights and preferences is to eliminate delays associated with a stockholder vote on specific issuances. Examples of rights and preferences that our Board of Directors may fix are:

- dividend rights;
- conversion rights;
- voting rights;
- terms of redemption;
- liquidation preferences;
- sinking fund terms; and
- the number of shares constituting, or the designation of, such series, any or all of which may be greater than the rights of common stock.

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. The rights of holders of our common stock described above, will be subject to, and may be adversely affected by, the rights of any preferred stock that we may designate and issue in the future. 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.

## **Warrants**

As of September 30, 2019, 477,639 shares of our common stock are issuable upon the exercise of warrants outstanding with a weighted average exercise price of \$64.95. As of December 31, 2019, warrants to purchase 463,735 shares of common stock expired pursuant to their respective terms.

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

Certain provisions of the Delaware General Corporation Law (DGCL) and of our amended and restated certificate of incorporation and 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. Generally, to be timely, notice must be received at our principal executive offices not less than 90 days nor more than 120 days prior to the first anniversary date of the annual meeting for the preceding year. Our amended and restated bylaws specify the requirements as to form and content of all stockholders' notices.

**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 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.

**Undesignated Preferred Stock.** Our amended and restated certificate of incorporation provides for 5,000,000 authorized shares of undesignated preferred stock, of which 2,285,952 shares have been designated as Class X Convertible Preferred Stock. Our other classes of designated preferred stock may not be issued. The existence of authorized but unissued shares of undesignated preferred stock may enable our Board of Directors 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 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 or insurgent stockholder or stockholder group. In this regard, our certificate of incorporation grants our Board of Directors broad power to establish the rights and preferences of authorized and unissued shares of preferred 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.

**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 certificate of incorporation or our 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 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.

## MATERIAL UNITED STATES FEDERAL INCOME TAX CONSEQUENCES TO NON-U.S. HOLDERS OF OUR COMMON STOCK

The following is a summary of the material U.S. federal income tax consequences to non-U.S. holders (as defined below) of the acquisition, ownership and disposition of our common stock issued pursuant to this offering. This discussion is not a complete analysis of all potential U.S. federal income tax consequences relating thereto, does not address the potential application of the Medicare contribution tax on net investment income, and does not address any estate or gift tax consequences or any tax consequences arising under any state, local or foreign tax laws, or any other U.S. federal tax laws. This discussion is based on the Internal Revenue Code of 1986, as amended (the Code) and applicable Treasury Regulations promulgated thereunder, judicial decisions and published rulings and administrative pronouncements of the Internal Revenue Service (IRS) all as in effect as of the date hereof. These authorities are subject to differing interpretations and may change, possibly retroactively, resulting in U.S. federal income tax consequences different from those discussed below. We have not requested a ruling from the IRS with respect to the statements made and the conclusions reached in the following summary, and there can be no assurance that the IRS or a court will agree with such statements and conclusions.

This discussion is limited to non-U.S. holders who purchase our common stock pursuant to this offering and who hold our common stock as a “capital asset” within the meaning of Section 1221 of the Code (generally, property held for investment). This discussion does not address all of the U.S. federal income tax consequences that may be relevant to a particular holder in light of such holder’s particular circumstances. This discussion also does not consider any specific facts or circumstances that may be relevant to holders subject to special rules under the U.S. federal income tax laws, including:

- certain former citizens or long-term residents of the United States;
- partnerships or other pass-through entities (and investors therein);
- “controlled foreign corporations;”
- “passive foreign investment companies;”
- corporations that accumulate earnings to avoid U.S. federal income tax;
- banks, financial institutions, investment funds, insurance companies, brokers, dealers or traders in securities;
- tax-exempt organizations and governmental organizations;
- tax-qualified retirement plans;
- persons subject to the alternative minimum tax;
- persons that own, or have owned, actually or constructively, more than 5% of our common stock;
- accrual-method taxpayers subject to special tax accounting rules under Section 451(b) of the Code;
- persons who have elected to mark securities to market;
- persons who hold or receive our common stock pursuant to the exercise of any option or otherwise as compensation;
- “qualified foreign pension funds” as defined in Section 897(l)(2) of the Code and entities all of the interests of which are held by qualified foreign pension funds; and
- persons holding our common stock as part of a hedging or conversion transaction or straddle, or a constructive sale, or other risk reduction strategy or integrated investment.

If an entity or arrangement that is classified as a partnership for U.S. federal income tax purposes holds our common stock, the U.S. federal income tax treatment of a partner in the partnership will generally depend on the status of the partner and the activities of the partnership. Partnerships holding our common stock and the partners in such partnerships are urged to consult their tax advisors about the particular U.S. federal income tax consequences to them of holding and disposing of our common stock.

**THIS DISCUSSION IS FOR INFORMATIONAL PURPOSES ONLY AND IS NOT TAX ADVICE. PROSPECTIVE INVESTORS SHOULD CONSULT THEIR TAX ADVISORS REGARDING THE PARTICULAR U.S. FEDERAL INCOME TAX CONSEQUENCES TO THEM OF ACQUIRING, OWNING AND DISPOSING OF OUR COMMON STOCK, AS WELL AS ANY TAX CONSEQUENCES ARISING UNDER ANY STATE, LOCAL OR FOREIGN TAX LAWS AND ANY OTHER U.S. FEDERAL TAX LAWS. YOU SHOULD ALSO CONSULT WITH YOUR TAX ADVISOR WITH RESPECT TO SUCH CHANGES IN U.S. TAX LAW AS WELL AS POTENTIAL CONFORMING CHANGES IN STATE TAX LAWS.**

#### **Definition of Non-U.S. Holder**

For purposes of this discussion, a non-U.S. holder is any beneficial owner of our common stock that is not a “U.S. person” or a partnership (including any entity or arrangement treated as a partnership) for U.S. federal income tax purposes. A U.S. person is any person that, for U.S. federal income tax purposes, is or is treated as any of the following:

- an individual who is a citizen or resident of the United States;
- a corporation (or entity treated as a corporation for U.S. federal income tax purposes) created or organized under the laws of the United States, any state thereof or the District of Columbia;
- an estate, the income of which is subject to U.S. federal income tax regardless of its source; or
- a trust (1) whose administration is subject to the primary supervision of a U.S. court and which has one or more U.S. persons who have the authority to control all substantial decisions of the trust or (2) that has a valid election in effect under applicable Treasury Regulations to be treated as a U.S. person.

#### **Distributions on Our Common Stock**

As described under the section titled “Dividend Policy,” we have not paid and do not anticipate paying dividends. However, if we make cash or other property distributions on our common stock, such distributions will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. Amounts not treated as dividends for U.S. federal income tax purposes will constitute a return of capital and will first be applied against and reduce a non-U.S. holder’s tax basis in our common stock, but not below zero. Any excess will be treated as gain realized on the sale or other disposition of our common stock and will be treated as described under the section titled “—Gain on Disposition of Our Common Stock” below.

Subject to the discussions below regarding effectively connected income, backup withholding and Sections 1471 through 1474 of the Code (commonly referred to as FATCA), dividends paid to a non-U.S. holder of our common stock generally will be subject to U.S. federal withholding tax at a rate of 30% of the gross amount of the dividends or such lower rate specified by an applicable income tax treaty. To receive the benefit of a reduced treaty rate, a non-U.S. holder must furnish us or our paying agent with a valid IRS Form W-8BEN or IRS Form W-8BEN-E (or applicable successor form) and satisfy applicable certification and other requirements. This certification must be provided to us or our paying agent before the payment of dividends and must be updated periodically. If the non-U.S. holder holds the stock through a financial institution or other agent acting on the non-U.S. holder’s behalf, the non-U.S. holder will be required to provide appropriate documentation to the agent, which then will be required to provide certification to us or our paying agent, either directly or through other intermediaries.

If a non-U.S. holder holds our common stock in connection with the conduct of a trade or business in the United States, and dividends paid on our common stock are effectively connected with such holder’s U.S. trade or business (and are attributable to such holder’s permanent establishment in the United States if required by an applicable tax treaty), the non-U.S. holder will be exempt from U.S. federal withholding tax. To claim the exemption, the non-U.S. holder must generally furnish a valid IRS Form W-8ECI (or applicable successor form) to the applicable withholding agent.

However, any such effectively connected dividends paid on our common stock generally will be subject to U.S. federal income tax on a net income basis at the regular U.S. federal income tax rates in the same manner as if such holder were a resident of the United States. A non-U.S. holder that is a foreign corporation also may be subject to an additional branch profits tax equal to 30% (or such lower rate specified by an applicable income tax treaty) of its effectively connected earnings and profits for the taxable year, as adjusted for certain items. Non-U.S. holders should consult their tax advisors regarding any applicable income tax treaties that may provide for different rules.

Non-U.S. holders that do not provide the required certification on a timely basis, but that qualify for a reduced treaty rate, may obtain a refund of any excess amounts withheld by timely filing an appropriate claim for refund with the IRS.

### **Gain on Disposition of Our Common Stock**

Subject to the discussions below regarding backup withholding and FATCA, a non-U.S. holder generally will not be subject to U.S. federal income tax on any gain realized on the sale or other disposition of our common stock, unless:

- the gain is effectively connected with the non-U.S. holder's conduct of a trade or business in the United States, and if required by an applicable income tax treaty, is attributable to a permanent establishment maintained by the non-U.S. holder in the United States;
- the non-U.S. holder is a nonresident alien individual present in the United States for 183 days or more during the taxable year of the disposition, and certain other requirements are met; or
- our common stock constitutes a "United States real property interest" by reason of our status as a United States real property holding corporation (USRPHC), for U.S. federal income tax purposes at any time within the shorter of the five-year period preceding the disposition or the non-U.S. holder's holding period for our common stock, and our common stock is not regularly traded on an established securities market during the calendar year in which the sale or other disposition occurs.

If we are a USRPHC and either our common stock is not regularly traded on an established securities market or a non-U.S. holder holds, or is treated as holding, more than 5% of our outstanding common stock, directly or indirectly, during the applicable testing period, gain described in the third bullet point above will generally be taxed in the same manner as gain that is effectively connected with the conduct of a U.S. trade or business, except that the branch profits tax generally will not apply. Determining whether we are a USRPHC depends on the fair market value of our U.S. real property interests relative to the fair market value of our other trade or business assets and our foreign real property interests. We believe that we are not currently and do not anticipate becoming a USRPHC for U.S. federal income tax purposes, although there can be no assurance we will not in the future become a USRPHC. If we are a USRPHC and our common stock is not regularly traded on an established securities market, a non-U.S. holder's proceeds received on the disposition of shares will also generally be subject to withholding at a rate of 15%. Prospective investors are encouraged to consult their own tax advisors regarding the possible consequences to them if we are, or were to become, a USRPHC.

Gain described in the first bullet point above generally will be subject to U.S. federal income tax on a net income basis at the regular U.S. federal income tax rates in the same manner as if such holder were a resident of the United States. A non-U.S. holder that is a foreign corporation also may be subject to an additional branch profits tax equal to 30% (or such lower rate specified by an applicable income tax treaty) of its effectively connected earnings and profits for the taxable year, as adjusted for certain items.

Gain described in the second bullet point above will be subject to U.S. federal income tax at a flat 30% rate (or such lower rate specified by an applicable income tax treaty), but may be offset by certain U.S.-source capital losses (even though the individual is not considered a resident of the United States), provided that the non-U.S. holder has timely filed U.S. federal income tax returns with respect to such losses. Non-U.S. holders should consult their tax advisors regarding any applicable income tax treaties that may provide for different rules.

### **Information Reporting and Backup Withholding**

Annual reports are required to be filed with the IRS and provided to each non-U.S. holder indicating the amount of dividends on our common stock paid to such holder and the amount of any tax withheld with respect to those dividends. These information reporting requirements apply even if no withholding was required because the dividends were effectively connected with the holder's conduct of a U.S. trade or business, or withholding was reduced or eliminated by an applicable income tax treaty. This information also may be made available under a specific treaty or agreement with the tax authorities in the country in which the non-U.S. holder resides or is established. Backup withholding, currently at a 24% rate, generally will not apply to payments to a non-U.S. holder of dividends on or the gross proceeds of a disposition of our common stock provided the non-U.S. holder furnishes the required certification for its non-U.S. status, such as by providing a valid IRS Form W-8BEN, IRS Form W-8BEN-E or IRS Form W-8ECI, or certain other requirements are met. Backup withholding may apply if the payor has actual knowledge, or reason to know, that the holder is a U.S. person who is not an exempt recipient.

Backup withholding is not an additional tax. If any amount is withheld under the backup withholding rules, the non-U.S. holder should consult with a U.S. tax advisor regarding the possibility of and procedure for obtaining a refund or a credit against the non-U.S. holder's U.S. federal income tax liability, if any.

## **Withholding on Foreign Entities**

FATCA imposes a U.S. federal withholding tax of 30% on certain payments made to a “foreign financial institution” (as specially defined under these rules) unless such institution enters into an agreement with the U.S. government to withhold on certain payments and to collect and provide to the U.S. tax authorities substantial information regarding certain U.S. account holders of such institution (which includes certain equity and debt holders of such institution, as well as certain account holders that are foreign entities with U.S. owners) or an exemption applies. FATCA also generally will impose a U.S. federal withholding tax of 30% on certain payments made to a non-financial foreign entity unless such entity provides the withholding agent a certification identifying certain direct and indirect U.S. owners of the entity or an exemption applies. An intergovernmental agreement between the United States and an applicable foreign country may modify these requirements. Under certain circumstances, a non-U.S. holder might be eligible for refunds or credits of such taxes. FATCA currently applies to dividends paid on our common stock. Under applicable Treasury Regulations and administrative guidance, withholding under FATCA would have applied to payments of gross proceeds from the sale or other disposition of stock on or after January 1, 2019, but under proposed regulations (the preamble to which specifies that taxpayers are permitted to rely on such proposed regulations pending finalization), no withholding would apply with respect to payments of gross proceeds.

Prospective investors are encouraged to consult with their own tax advisors regarding the possible implications of this legislation on their investment in our common stock.

## UNDERWRITING

We entered into an underwriting agreement with the underwriters named below on February 5, 2020. Oppenheimer & Co. Inc. is acting as the sole book-running manager and representative of the underwriters. The underwriting agreement provides for the purchase of a specific number of shares of common stock by each of the underwriters. The underwriters' obligations are several, which means that each underwriter is required to purchase a specified number of shares, but is not responsible for the commitment of any other underwriter to purchase shares. Subject to the terms and conditions of the underwriting agreement, each underwriter has severally agreed to purchase the number of shares set forth opposite its name below:

<b>Underwriter</b>	<b>Number of Shares of Common Stock</b>
Oppenheimer & Co. Inc.	3,176,471
Roth Capital Partners, LLC	1,058,823
<b>Total</b>	<b>4,235,294</b>

The underwriters have agreed to purchase all of the shares offered by this prospectus (other than those covered by the over-allotment option described below), if any are purchased.

The shares of common stock offered hereby are expected to be ready for delivery on or about February 10, 2020 against payment in immediately available funds.

The underwriters are offering the shares subject to various conditions and may reject all or part of any order. The representative of the underwriters has advised us that the underwriters propose initially to offer the shares of common stock to the public at the public offering price set forth on the cover page of this prospectus and to dealers at a price less a concession not in excess of \$0.1785 per share to brokers and dealers. After the shares are released for sale to the public, the representative may change the offering price, the concession, and other selling terms at various times.

We have granted the underwriters an over-allotment option. This option, which is exercisable for up to 30 days after the date of this prospectus, permits the underwriters to purchase a maximum of 635,294 additional shares of common stock from us to cover over-allotments, if any. If the underwriters exercise all or part of this option, they will purchase shares of common stock covered by the option at the public offering price that appears on the cover page of this prospectus, less the underwriting discounts and commissions. If this option is exercised in full, the total price to public will be \$20.7 million, and the total proceeds to us, before expenses, will be \$19.3 million.

The following table provides information regarding the amount of the discounts and commissions to be paid to the underwriters by us, before expenses:

	<b>Per Share of Common Stock</b>	<b>Total without Exercise of Over-Allotment Option</b>	<b>Total with Full Exercise of Over- Allotment Option</b>
Public offering price	\$ 4.25	\$ 18,000,000	\$ 20,699,999
Underwriting discounts and commissions <sup>(1)</sup>	\$ 0.2975	\$ 1,260,000	\$ 1,449,000
Proceeds, before expenses, to us	\$ 3.9525	\$ 16,740,000	\$ 19,250,999

(1) We have agreed to pay the underwriters a commission of 7% of the gross proceeds of this offering.

We estimate that our total expenses of the offering, excluding the underwriting discounts and commissions, will be approximately \$0.5 million, which includes the fees and expenses for which we have agreed to reimburse the underwriters, provided that such fees and expenses shall not exceed an aggregate of \$100,000.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act of 1933. For a period of six (6) months following the closing of this offering, the representative has a right of first refusal to act as an underwriter, placement agent, or the like, as applicable, in connection with any equity financing in which we engage any such advisors and that results in gross proceeds of at least \$10.0 million.

We and our officers and directors have agreed to a 90-day "lock-up" each with respect to shares of our common stock and other of our securities that they beneficially own, including securities that are convertible into shares of common stock and securities that are exchangeable or exercisable for shares of common stock. This means that, subject to certain exceptions, for a period of 90 days following



the date of this prospectus, as applicable, we and such persons or entities may not offer, sell, pledge or otherwise dispose of these securities without the prior written consent of Oppenheimer & Co. Inc.

Paul Schimmel, Ph.D., a stockholder and member of our Board of Directors, has indicated an interest in purchasing up to a number of shares of the common stock offered in this offering as would maintain his current pro-rata percentage ownership of our common stock. Because indications of interest are not binding agreements or commitments to purchase, he may determine to purchase fewer or more shares than he has indicated an interest in purchasing, or elect not to purchase any shares in this offering. The underwriters may also determine to sell fewer, more or no shares in this offering to him.

Rules of the Securities and Exchange Commission may limit the ability of the underwriters to bid for or purchase shares before the distribution of the shares is completed. However, the underwriters may engage in the following activities in accordance with the rules:

- Stabilizing transactions - the representative may make bids or purchases for the purpose of pegging, fixing or maintaining the price of the shares, so long as stabilizing bids do not exceed a specified maximum.
- Over-allotments and syndicate covering transactions - the underwriters may sell more shares of common stock in connection with this offering than the number of shares of common stock that they have committed to purchase. This over-allotment creates a short position for the underwriters. This short sales position may involve either "covered" short sales or "naked" short sales. Covered short sales are short sales made in an amount not greater than the underwriters' over-allotment option to purchase additional shares of common stock in this offering described above. The underwriters may close out any covered short position either by exercising its over-allotment option or by purchasing shares of common stock in the open market. To determine how they will close the covered short position, the underwriters will consider, among other things, the price per share of common stock available for purchase in the open market, as compared to the price at which they may purchase shares of common stock through the over-allotment option. Naked short sales are short sales in excess of the over-allotment option. The underwriters must close out any naked short position by purchasing shares of common stock in the open market. A naked short position is more likely to be created if the underwriters are concerned that, in the open market after pricing, there may be downward pressure on the price per share of common stock that could adversely affect investors who purchase shares of common stock in this offering.
- Penalty bids - if the representative purchases shares in the open market in a stabilizing transaction or syndicate covering transaction, it may reclaim a selling concession from the underwriters and selling group members who sold those shares as part of this offering.
- Passive market making - market makers in the shares who are underwriters or prospective underwriters may make bids for or purchases of shares, subject to limitations, until the time, if ever, at which a stabilizing bid is made.

Similar to other purchase transactions, the underwriters' purchases to cover the syndicate short sales or to stabilize the market price of our common stock may have the effect of raising or maintaining the market price of our common stock or preventing or mitigating a decline in the market price of our common stock. As a result, the price of the shares of our common stock may be higher than the price that might otherwise exist in the open market. The imposition of a penalty bid might also have an effect on the price of the shares if it discourages resales of the shares.

Neither we nor the underwriters make any representation or prediction as to the effect that the transactions described above may have on the price of the shares. These transactions may occur on the Nasdaq Capital Market or otherwise. If such transactions are commenced, they may be discontinued without notice at any time.

Electronic Delivery of Prospectus: A prospectus in electronic format may be delivered to potential investors by one or more of the underwriters participating in this offering. The prospectus in electronic format will be identical to the paper version of such prospectus. Other than the prospectus in electronic format, the information on any underwriter's website and any information contained in any other website maintained by an underwriter is not part of this prospectus or the registration statement of which this prospectus forms a part.

#### **Notice to Non-U.S. Investors**

##### *Belgium*

The offering is exclusively conducted under applicable private placement exemptions and therefore it has not been and will not be notified to, and this document or any other offering material relating to the shares has not been and will not be approved by, the

Belgian Banking, Finance and Insurance Commission (Commission bancaire, financière et des assurances/Commissie voor het Bank, Financie en Assurantiewezen). Any representation to the contrary is unlawful.

Each underwriter has undertaken not to offer sell, resell, transfer or deliver directly or indirectly, any shares, or to take any steps relating/ancillary thereto, and not to distribute or publish this document or any other material relating to the shares or to the offering in a manner which would be construed as: (a) a public offering under the Belgian Royal Decree of 7 July 1999 on the public character of financial transactions; or (b) an offering of securities to the public under Directive 2003/71/EC which triggers an obligation to publish a prospectus in Belgium. Any action contrary to these restrictions will cause the recipient and the company to be in violation of the Belgian securities laws.

#### *Canada*

This document constitutes an “exempt offering document” as defined in and for the purposes of applicable Canadian securities laws. No prospectus has been filed with any securities commission or similar regulatory authority in Canada in connection with the offer and sale of the securities described herein (the Securities). No securities commission or similar regulatory authority in Canada has reviewed or in any way passed upon this document or on the merits of the Securities and any representation to the contrary is an offence.

**Canadian investors are advised that this document has been prepared in reliance on section 3A.3 of National Instrument 33-105 Underwriting Conflicts (NI 33-105). Pursuant to section 3A.3 of NI 33-105, this document is exempt from the requirement to provide investors with certain conflicts of interest disclosure pertaining to “connected issuer” and/or “related issuer” relationships as would otherwise be required pursuant to subsection 2.1(1) of NI 33-105.**

#### **Resale Restrictions**

The offer and sale of the securities in Canada is being made on a private placement basis only and is exempt from the requirement to prepare and file a prospectus under applicable Canadian securities laws. Any resale of Securities acquired by a Canadian investor in this offering must be made in accordance with applicable Canadian securities laws, which may vary depending on the relevant jurisdiction, and which may require resales to be made in accordance with Canadian prospectus requirements, a statutory exemption from the prospectus requirements, in a transaction exempt from the prospectus requirements or otherwise under a discretionary exemption from the prospectus requirements granted by the applicable local Canadian securities regulatory authority. These resale restrictions may under certain circumstances apply to resales of the Securities outside of Canada.

#### **Representations of Purchasers**

Each Canadian investor who purchases the securities will be deemed to have represented to the issuer and to each dealer from whom a purchase confirmation is received, as applicable, that the investor (i) is purchasing as principal, or is deemed to be purchasing as principal in accordance with applicable Canadian securities laws, for investment only and not with a view to resale or redistribution; (ii) is an “accredited investor” as such term is defined in section 1.1 of National Instrument 45-106 *Prospectus Exemptions* (NI 45-106) or, in Ontario, as such term is defined in section 73.3(1) of the *Securities Act* (Ontario); and (iii) is a “permitted client” as such term is defined in section 1.1 of National Instrument 31-103 *Registration Requirements, Exemptions and Ongoing Registrant Obligations*.

#### **Taxation and Eligibility for Investment**

Any discussion of taxation and related matters contained in this document does not purport to be a comprehensive description of all of the tax considerations that may be relevant to a Canadian investor when deciding to purchase the securities and, in particular, does not address any Canadian tax considerations. No representation or warranty is hereby made as to the tax consequences to a resident, or deemed resident, of Canada of an investment in the securities or with respect to the eligibility of the securities for investment by such investor under relevant Canadian federal and provincial legislation and regulations.

#### **Rights of Action for Damages or Rescission**

Securities legislation in certain of the Canadian jurisdictions provides certain purchasers of securities pursuant to an offering memorandum, including where the distribution involves an “eligible foreign security” as such term is defined in Ontario Securities Commission Rule 45-501 *Ontario Prospectus and Registration Exemptions* and in Multilateral Instrument 45-107 *Listing Representation and Statutory Rights of Action Disclosure Exemptions*, as applicable, with a remedy for damages or rescission, or both, in addition to any other rights they may have at law, where the offering memorandum, or other offering document that constitutes an offering memorandum, and any amendment thereto, contains a “misrepresentation” as defined under applicable Canadian securities laws. These remedies, or notice with respect to these remedies, must be exercised or delivered, as the case may be, by the purchaser

within the time limits prescribed under, and are subject to limitations and defences under, applicable Canadian securities legislation. In addition, these remedies are in addition to and without derogation from any other right or remedy available at law to the investor.

## Language of Documents

Upon receipt of this document, each Canadian investor hereby confirms that it has expressly requested that all documents evidencing or relating in any way to the sale of the securities described herein (including for greater certainty any purchase confirmation or any notice) be drawn up in the English language only. *Par la réception de ce document, chaque investisseur canadien confirme par les présentes qu'il a expressément exigé que tous les documents faisant foi ou se rapportant de quelque manière que ce soit à la vente des valeurs mobilières décrites aux présentes (incluant, pour plus de certitude, toute confirmation d'achat ou tout avis) soient rédigés en anglais seulement.*

### France

Neither this prospectus nor any other offering material relating to the shares has been submitted to the clearance procedures of the Autorité des marchés financiers in France. The shares have not been offered or sold and will not be offered or sold, directly or indirectly, to the public in France. Neither this prospectus nor any other offering material relating to the shares has been or will be: (a) released, issued, distributed or caused to be released, issued or distributed to the public in France; or (b) used in connection with any offer for subscription or sale of the shares to the public in France. Such offers, sales and distributions will be made in France only: (i) to qualified investors (investisseurs qualifiés) and/or to a restricted circle of investors (cercle restreint d'investisseurs), in each case investing for their own account, all as defined in and in accordance with Articles L.411-2, D.411-1, D.411-2, D.734-1, D.744-1, D.754-1 and D.764-1 of the French Code monétaire et financier; (ii) to investment services providers authorised to engage in portfolio management on behalf of third parties; or (iii) in a transaction that, in accordance with article L.411-2-II-1<sup>o</sup>-or-2<sup>o</sup>-or 3<sup>o</sup> of the French Code monétaire et financier and article 211-2 of the General Regulations (Règlement Général) of the Autorité des marchés financiers, does not constitute a public offer (appel public à l'épargne). Such shares may be resold only in compliance with Articles L.411-1, L.411-2, L.412-1 and L.621-8 through L.621-8-3 of the French Code monétaire et financier.

### United Kingdom/Germany/Norway/The Netherlands

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a Relevant Member State) an offer to the public of any shares which are the subject of the offering contemplated by this prospectus may not be made in that Relevant Member State other than the offers contemplated in this prospectus in name(s) of Member State(s) where prospectus will be approved or passported for the purposes of a non-exempt offer once this prospectus has been approved by the competent authority in such Member State and published and passported in accordance with the Prospectus Directive as implemented in name(s) of relevant Member State(s) except that an offer to the public in that Relevant Member State of any shares may be made at any time under the following exemptions under the Prospectus Directive, if they have been implemented in that Relevant Member State:

- (a) to legal entities which are authorised or regulated to operate in the financial markets or, if not so authorised or regulated, whose corporate purpose is solely to invest in securities;
- (b) to any legal entity which has two or more of (1) an average of at least 250 employees during the last financial year; (2) a total balance sheet of more than €43,000,000 and (3) an annual net turnover of more than €50,000,000, as shown in its last annual or consolidated accounts;
- (c) by the representative to fewer than 100 natural or legal persons (other than qualified investors as defined in the Prospectus Directive); or
- (d) in any other circumstances falling within Article 3(2) of the Prospectus Directive, provided that no such offer of shares shall result in a requirement for the publication by the company or any underwriter of a prospectus pursuant to Article 3 of the Prospectus Directive.

For the purposes of this provision, the expression an "offer to the public" in relation to any shares in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and any shares to be offered so as to enable an investor to decide to purchase any shares, as the same may be varied in that Member State by any measure implementing the Prospectus Directive in that Member State and the expression "Prospectus Directive" means Directive 2003/71/EC and includes any relevant implementing measure in each Relevant Member State.

Each underwriter has represented, warranted and agreed that:

- (a) it has only communicated or caused to be communicated and will only communicate or cause to be communicated any invitation or inducement to engage in investment activity (within the meaning of section 21 of the Financial Services and Markets Act 2000

(the FSMA)) received by it in connection with the issue or sale of any shares in circumstances in which section 21(1) of the FSMA does not apply to the company; and

- (b) it has complied with and will comply with all applicable provisions of the FSMA with respect to anything done by it in relation to the shares in, from or otherwise involving the United Kingdom.

#### *Israel*

In the State of Israel, the shares offered hereby may not be offered to any person or entity other than the following:

- (a) a fund for joint investments in trust (i.e., mutual fund), as such term is defined in the Law for Joint Investments in Trust, 5754-1994, or a management company of such a fund;
- (b) a provident fund as defined in Section 47(a)(2) of the Income Tax Ordinance of the State of Israel, or a management company of such a fund;
- (c) an insurer, as defined in the Law for Oversight of Insurance Transactions, 5741-1981, (d) a banking entity or satellite entity, as such terms are defined in the Banking Law (Licensing), 5741-1981, other than a joint services company, acting for their own account or for the account of investors of the type listed in Section 15A(b) of the Securities Law 1968;
- (d) a company that is licensed as a portfolio manager, as such term is defined in Section 8(b) of the Law for the Regulation of Investment Advisors and Portfolio Managers, 5755-1995, acting on its own account or for the account of investors of the type listed in Section 15A(b) of the Securities Law 1968;
- (e) a company that is licensed as an investment advisor, as such term is defined in Section 7(c) of the Law for the Regulation of Investment Advisors and Portfolio Managers, 5755-1995, acting on its own account;
- (f) a company that is a member of the Tel Aviv Stock Exchange, acting on its own account or for the account of investors of the type listed in Section 15A(b) of the Securities Law 1968;
- (g) an underwriter fulfilling the conditions of Section 56(c) of the Securities Law, 5728-1968;
- (h) a venture capital fund (defined as an entity primarily involved in investments in companies which, at the time of investment, (i) are primarily engaged in research and development or manufacture of new technological products or processes and (ii) involve above-average risk);
- (i) an entity primarily engaged in capital markets activities in which all of the equity owners meet one or more of the above criteria; and
- (j) an entity, other than an entity formed for the purpose of purchasing shares in this offering, in which the shareholders equity (including pursuant to foreign accounting rules, international accounting regulations and U.S. generally accepted accounting rules, as defined in the Securities Law Regulations (Preparation of Annual Financial Statements), 1993) is in excess of NIS 50 million.

Any offeree of the shares offered hereby in the State of Israel shall be required to submit written confirmation that it falls within the scope of one of the above criteria. This prospectus will not be distributed or directed to investors in the State of Israel who do not fall within one of the above criteria.

#### *Italy*

The offering of the shares offered hereby in Italy has not been registered with the Commissione Nazionale per la Società e la Borsa (CONSOB) pursuant to Italian securities legislation and, accordingly, the shares offered hereby cannot be offered, sold or delivered in the Republic of Italy (Italy) nor may any copy of this prospectus or any other document relating to the shares offered hereby be distributed in Italy other than to professional investors (operatori qualificati) as defined in Article 31, second paragraph, of CONSOB Regulation No. 11522 of 1 July, 1998 as subsequently amended. Any offer, sale or delivery of the shares offered hereby or distribution of copies of this prospectus or any other document relating to the shares offered hereby in Italy must be made:

- (a) by an investment firm, bank or intermediary permitted to conduct such activities in Italy in accordance with Legislative Decree No. 58 of 24 February 1998 and Legislative Decree No. 385 of 1 September 1993 (the Banking Act);
- (b) in compliance with Article 129 of the Banking Act and the implementing guidelines of the Bank of Italy; and
- (c) in compliance with any other applicable laws and regulations and other possible requirements or limitations which may be imposed by Italian authorities.

### *Sweden*

This prospectus has not been nor will it be registered with or approved by Finansinspektionen (the Swedish Financial Supervisory Authority). Accordingly, this prospectus may not be made available, nor may the shares offered hereunder be marketed and offered for sale in Sweden, other than under circumstances which are deemed not to require a prospectus under the Financial Instruments Trading Act (1991: 980).

### *Switzerland*

The shares offered pursuant to this prospectus will not be offered, directly or indirectly, to the public in Switzerland and this prospectus does not constitute a public offering prospectus as that term is understood pursuant to art. 652a or art. 1156 of the Swiss Federal Code of Obligations. The company has not applied for a listing of the shares being offered pursuant to this prospectus on the SWX Swiss Exchange or on any other regulated securities market, and consequently, the information presented in this prospectus does not necessarily comply with the information standards set out in the relevant listing rules. The shares being offered pursuant to this prospectus have not been registered with the Swiss Federal Banking Commission as foreign investment funds, and the investor protection afforded to acquirers of investment fund certificates does not extend to acquirers of shares.

Investors are advised to contact their legal, financial or tax advisers to obtain an independent assessment of the financial and tax consequences of an investment in shares.

## LEGAL MATTERS

The validity of the shares of common stock being offered by this prospectus will be passed upon for us by Cooley LLP, San Diego, California. Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., New York, New York, is acting as counsel for the underwriters.

## EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements at December 31, 2018 and 2017 and for each of the three years in the period ended December 31, 2018, as set forth in their report. We have included our consolidated financial statements in the prospectus and elsewhere in this registration statement in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

## WHERE YOU CAN FIND MORE INFORMATION

We have filed with the SEC a registration statement on Form S-1 under the Securities Act with respect to the shares of common stock offered hereby. This prospectus, which constitutes a part of the registration statement, does not contain all of the information set forth in the registration statement or the exhibits and schedules filed therewith. For further information about us and the common stock offered hereby, we refer you to the registration statement and the exhibits filed thereto. Statements contained in this prospectus regarding the contents of any contract or any other document that is filed as an exhibit to the registration statement are not necessarily complete, and each such statement is qualified in all respects by reference to the full text of such contract or other document filed as an exhibit to the registration statement. We are required to file periodic reports, proxy statements and other information with the SEC pursuant to the Exchange Act. The SEC maintains an Internet website that contains reports, proxy statements and other information about registrants, like us, that file electronically with the SEC. The address of that site is <http://www.sec.gov>.

We file periodic reports, proxy statements and other information with the SEC. Such periodic reports, proxy statements and other information will be available at the website of the SEC referred to above. We maintain a website at [www.atyrpharma.com](http://www.atyrpharma.com). You may access our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act with the SEC free of charge at our website as soon as reasonably practicable after such material is electronically filed with, or furnished to, the SEC. The reference to our website address does not constitute incorporation by reference of the information contained on our website, and you should not consider the contents of our website in making an investment decision with respect to our common stock.

**aTyr Pharma, Inc.**  
**FINANCIAL STATEMENTS**  
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## 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, 2018 and 2017, 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, 2018, 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, 2018 and 2017, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2018, in conformity with U.S. generally accepted accounting principles.

### Basis for Opinion

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

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

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

/s/ Ernst & Young LLP

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

San Diego, California  
March 26, 2019,  
except for the fourth paragraph of Note 1, as to which the date is  
January 17, 2020



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

	<b>December 31,</b>	
	<b>2018</b>	<b>2017</b>
<b>Assets</b>		
Current assets:		
Cash and cash equivalents	\$ 22,962	\$ 21,091
Available-for-sale investments, short-term	26,583	64,028
Prepaid expenses and other assets	1,258	1,866
Total current assets	50,803	86,985
Property and equipment, net	1,853	2,280
Other assets	90	90
Total assets	\$ 52,746	\$ 89,355
<b>Liabilities and Stockholders' Equity</b>		
Current liabilities:		
Accounts payable	\$ 1,040	\$ 2,276
Accrued expenses	2,026	3,103
Current portion of long-term debt, net of issuance costs and discount	7,767	5,012
Total current liabilities	10,833	10,391
Long-term debt, net of current portion and issuance costs and discount	8,263	14,719
Commitments and contingencies (Note 5)		
Stockholders' equity:		
Preferred stock, \$0.001 par value; undesignated authorized shares – 5,000,000 at December 31, 2018 and 2017, respectively; Class X Convertible Preferred Stock issued and outstanding shares – 2,285,952 as of December 31, 2018 and 2017, respectively	2	2
Common stock, \$0.001 par value; authorized shares – 10,714,286 as of December 31, 2018 and 2017, respectively; issued and outstanding shares – 2,186,389 and 2,129,968 as of December 31, 2018 and 2017, respectively	31	30
Additional paid-in capital	332,378	328,519
Accumulated other comprehensive loss	(60)	(120)
Accumulated deficit	(298,701)	(264,186)
Total stockholders' equity	33,650	64,245
Total liabilities and stockholders' equity	\$ 52,746	\$ 89,355

*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>2018</b>	<b>2017</b>	<b>2016</b>
<b>Operating expenses:</b>			
Research and development	\$ 20,385	\$ 30,067	\$ 42,846
General and administrative	12,435	17,078	15,094
<b>Total operating expenses</b>	<b>32,820</b>	<b>47,145</b>	<b>57,940</b>
<b>Loss from operations</b>	<b>(32,820)</b>	<b>(47,145)</b>	<b>(57,940)</b>
<b>Other income (expense), net</b>			
Other income (expense), net	(1,695)	(1,062)	65
Loss on extinguishment of debt	—	—	(29)
<b>Total other income (expense), net</b>	<b>(1,695)</b>	<b>(1,062)</b>	<b>36</b>
<b>Loss before income taxes</b>	<b>(34,515)</b>	<b>(48,207)</b>	<b>(57,904)</b>
Income tax benefit	—	—	49
<b>Net loss</b>	<b>(34,515)</b>	<b>(48,207)</b>	<b>(57,855)</b>
<b>Net loss per share attributable to common stock holders, basic and diluted</b>	<b>\$ (16.11)</b>	<b>\$ (26.13)</b>	<b>\$ (34.16)</b>
<b>Weighted average common stock shares outstanding, basic and diluted</b>	<b>2,141,961</b>	<b>1,845,033</b>	<b>1,693,691</b>

*See accompanying notes.*

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

	<b>Years Ended December 31,</b>		
	<u>2018</u>	<u>2017</u>	<u>2016</u>
Net loss	\$ (34,515)	\$ (48,207)	\$ (57,855)
Other comprehensive gain (loss):			
Change in unrealized gain (loss) on available for sale investments, net of tax	60	(44)	95
Comprehensive loss	<u>\$ (34,455)</u>	<u>\$ (48,251)</u>	<u>\$ (57,760)</u>

*See accompanying notes.*

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

	Convertible Preferred Stock		Common Stock		Additional Paid-In Capital	Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount	Shares	Amount				
Balance as of December 31, 2015	—	—	1,692,912	24	273,321	(171)	(158,124)	115,050
Exercise of common stock options and release of restricted stock units	—	—	1,284	—	20	—	—	20
Issuance of common stock pursuant to employee stock purchase plan	—	—	4,056	—	143	—	—	143
Issuance of warrants related to term loan	—	—	—	—	217	—	—	217
Changes in share repurchase liability	—	—	—	—	102	—	—	102
Stock-based compensation	—	—	—	—	5,029	—	—	5,029
Net unrealized gain on investments, net of tax	—	—	—	—	—	95	—	95
Net loss	—	—	—	—	—	—	(57,855)	(57,855)
Balance as of December 31, 2016	—	—	1,698,252	\$ 24	\$ 278,832	\$ (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	6	42,231	—	—	42,239
Issuance of warrants related to term loan	—	—	—	—	263	—	—	263
Changes in share repurchase liability	—	—	—	—	48	—	—	48
Stock-based compensation	—	—	—	—	6,784	—	—	6,784
Net unrealized loss on investments, net of tax	—	—	—	—	—	(44)	—	(44)
Net loss	—	—	—	—	—	—	(48,207)	(48,207)
Balance as of December 31, 2017	2,285,952	2	2,129,968	\$ 30	\$ 328,519	\$ (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	1	378	—	—	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	\$ 31	\$ 332,378	\$ (60)	\$ (298,701)	\$ 33,650

*See accompanying notes.*

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

	<b>Years Ended December 31,</b>		
	<b>2018</b>	<b>2017</b>	<b>2016</b>
<b>Cash flows from operating activities:</b>			
Net loss	\$ (34,515)	\$ (48,207)	\$ (57,855)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	746	713	900
Stock-based compensation	3,431	6,784	5,029
Debt discount accretion and non-cash interest expense	966	590	173
Loss on debt extinguishment	—	—	29
Amortization (accretion) of premium (discount) of available-for-sale investment securities	(261)	14	531
Loss on disposal of property and equipment	18	—	—
Deferred rent	—	(130)	(315)
Changes in operating assets and liabilities			
Prepaid expenses and other assets	610	761	(421)
Accounts payable and accrued expenses	(2,058)	(2,889)	(932)
Net cash used in operating activities	<u>(31,063)</u>	<u>(42,364)</u>	<u>(52,861)</u>
<b>Cash flows from investing activities:</b>			
Purchases of property and equipment	(594)	(1,312)	(600)
Purchases of available-for-sale investment securities	(40,299)	(77,672)	(28,089)
Maturities of available-for-sale investment securities	78,065	51,347	62,216
Net cash provided by (used in) investing activities	<u>37,172</u>	<u>(27,637)</u>	<u>33,527</u>
<b>Cash flows from financing activities:</b>			
Proceeds from issuance of common stock through option exercises	14	186	20
Proceeds from issuance of common stock through at the market offerings, net of offering costs	379	—	—
Proceeds from issuance of common stock through employee purchase plan	36	175	143
Proceeds from borrowing, net	—	9,866	9,736
Repayment on borrowing	(4,667)	—	(5,202)
Proceeds from issuance of securities in the Private Placement, net of issuance cost	—	42,477	—
Net cash (used in) provided by financing activities	<u>(4,238)</u>	<u>52,704</u>	<u>4,697</u>
Net change in cash and cash equivalents	1,871	(17,297)	(14,637)
Cash and cash equivalents at beginning of period	21,091	38,388	53,025
Cash and cash equivalents at the end of period	<u>\$ 22,962</u>	<u>\$ 21,091</u>	<u>\$ 38,388</u>
<b>Supplemental disclosure of cash flow information:</b>			
Interest paid	<u>\$ 1,700</u>	<u>\$ 1,000</u>	<u>\$ 225</u>
Purchase of fixed assets included in accounts payable	<u>\$ 4</u>	<u>\$ 260</u>	<u>\$ —</u>
<b>Supplemental schedule of noncash investing and financing activities:</b>			
Issuance of warrants in connection with borrowings	<u>\$ —</u>	<u>\$ 263</u>	<u>\$ 217</u>
Changes in share repurchase liability	<u>\$ —</u>	<u>\$ 48</u>	<u>\$ 102</u>

See accompanying notes.

**Notes to Consolidated Financial Statements****1. Organization, Business and Basis of Presentation****Organization and Business**

We were incorporated in the state of Delaware on September 8, 2005. We are focused on the discovery and clinical development of innovative medicines based on novel immunological pathways.

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.

**Principles of Consolidation**

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

**Reverse Stock Split**

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. The accompanying consolidated financial statements and notes thereto 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.

**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 trials and research and development expenses. Although these estimates are based on our knowledge of current events and actions we may undertake in the future, actual results may ultimately differ materially from these estimates and assumptions.

**Segment Reporting**

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

**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, 2018, we held an aggregate total of \$26.6 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 approximately \$10,000 difference between the amortized cost and fair value of these investment securities. As of December 31, 2017, we held \$64.0 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 \$0.1 million difference between the amortized cost and fair value of these investment securities.

## **Concentration of Credit Risk**

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

## **Property and Equipment**

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

## **Impairment of Long-Lived Assets**

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

## **Accrued Expenses**

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

## **Research and Development Costs**

Research and development costs are expensed as incurred. Research and development costs include: salaries and employee-related expenses, including stock-based compensation and benefits for personnel in research and product development functions; costs associated with conducting our preclinical, development and regulatory activities, including fees paid to third-party professional consultants, service providers and our scientific, therapeutic and clinical 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 cost of the grant date fair value of employee stock option and restricted stock unit grants recognized over the requisite service period of the awards (usually the vesting period) on a straight-line basis. We recognize forfeitures as they occur as a reduction of expense. For stock option grants with performance-based milestones, the expense is recorded over the service period after the achievement of the milestone is probable or the performance condition is achieved. For stock option grants with market-based conditions, the expense is recorded using the accelerated attribution method over the requisite service period for each vesting tranche. We account for stock options granted to non-employees using the fair value approach. These option grants are subject to periodic revaluation over their vesting terms. We estimate the fair value of employee and non-employee stock option grants using the Black-Scholes option pricing model. We estimate the fair value of the market-based stock option grants using a Monte Carlo simulation. The fair value of restricted stock units is determined by the closing price as of the grant date.

## Income Taxes

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

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

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

On December 22, 2017, the U.S. enacted the Tax Cuts and Jobs Act (TCJA), which among other provisions, reduced the U.S. corporate tax rate from 35% to 21%, effective January 1, 2018. Due to the timing of the enactment and the complexity involved in applying the provisions of the TCJA, we made reasonable estimates of the effects and recorded provisional amounts, offset with valuation allowances, in its financial statements as of December 31, 2017. At December 31, 2018, we had completed our assessment of the impact of the TCJA and has reflected the impact in the current year. At December 31, 2018, there were no material changes from the provisional amounts recorded for the year ended December 31, 2017.

## Net Loss Per Share

Basic net loss per share is calculated by dividing the net loss attributable to common stockholders by the weighted average number of common shares outstanding for the period, without consideration for common stock equivalents and adjusted for the weighted average number of common shares outstanding that are subject to repurchase. We have excluded no shares, 261 and 1,860 shares subject to repurchase from the weighted average number of common shares outstanding for the years ended December 31, 2018, 2017 and 2016, respectively. Diluted net loss per share attributable to common stockholders is calculated by dividing the net loss attributable to common stockholders by the weighted average number of common stock equivalents outstanding for the period determined using the treasury-stock method. Dilutive common stock equivalents are comprised of convertible preferred stock, warrants for common stock, options and restricted stock units outstanding under our stock option plan and estimated shares to be purchased under our employee stock purchase plan. For all periods presented, there is no difference in the number of shares used to calculate basic and diluted shares outstanding due to our net loss position.



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

	Year Ended December 31,		
	2018	2017	2016
Class X convertible preferred stock (if-converted)	816,851	816,851	—
Warrants for common stock	477,639	477,639	8,687
Common stock options and restricted stock units	371,823	333,154	291,052
Employee stock purchase plan	1,610	2,220	2,631
	<u>1,667,923</u>	<u>1,629,864</u>	<u>302,370</u>

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

	Year Ended December 31,		
	2018	2017	2016
<b>Numerator:</b>			
Consolidated net loss	\$ (34,515)	\$ (48,207)	\$ (57,855)
<b>Denominator:</b>			
Weighted average common shares outstanding	2,141,961	1,845,294	1,695,551
Weighted average common shares subject to repurchase	—	(261)	(1,860)
Weighted average common shares outstanding - basic and diluted	<u>2,141,961</u>	<u>1,845,033</u>	<u>1,693,691</u>
<b>Net loss per share - basic and diluted</b>	<u>\$ (16.11)</u>	<u>\$ (26.13)</u>	<u>\$ (34.16)</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. The new standard became effective for interim and annual periods beginning after December 15, 2018, with early adoption permitted, and is required to be adopted at the earliest period presented using a modified retrospective approach. We adopted ASU No. 2016-02 on January 1, 2019. We anticipate recognizing a right-of-use asset and lease liability on our consolidated balance sheet for the discounted value of future lease payments from the adoption of this ASU. We are currently evaluating the full impact that the adoption of ASU No. 2016-02 will have on our consolidated financial statements and related disclosures.

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 is effective for fiscal years beginning after December 15, 2018, including interim periods within that fiscal year. Early adoption is permitted, but no earlier than an entity's adoption date of Topic 606. We are currently evaluating the impact of ASU No. 2018-07 and do not expect the adoption of this guidance will 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 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 for public business entities. We 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, 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	—
Sub-total short-term investments	26,583	—	26,583	—
Total assets measured at fair value	\$ 42,602	\$ 16,019	\$ 26,583	\$ —
<b>As of December 31, 2017:</b>				
Assets:				
Current:				
Cash equivalents	\$ 9,070	\$ 9,070	\$ —	\$ —
Available-for-sale investments, short-term:				
Asset-backed securities	6,497	—	6,497	—
Commercial paper	21,943	—	21,943	—
Corporate debt securities	18,260	—	18,260	—
United States Treasury securities	17,328	17,328	—	—
Sub-total short-term investments	64,028	17,328	46,700	—
Total assets measured at fair value	\$ 73,098	\$ 26,398	\$ 46,700	\$ —

As of December 31, 2018 and 2017, available-for-sale investments are detailed as follows (in thousands):

	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
	\$ 26,593	\$ —	\$ (10)	\$ 26,583
	December 31, 2017			
	Gross Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Market Value
Available-for-sale investments, short-term:				
Asset-backed securities	\$ 6,501	\$ —	\$ (4)	\$ 6,497
Commercial paper	21,943	—	—	21,943
Corporate debt securities	18,286	—	(26)	18,260
United States Treasury securities	17,368	—	(40)	17,328
	\$ 64,098	\$ —	\$ (70)	\$ 64,028

As of December 31, 2018, all available-for-sale investments have contractual maturity dates less than one year. As of December 31, 2018, all available-for-sale investments are in a gross unrealized loss position, and they have been in such position for less than twelve months.

At each reporting date, we perform an evaluation of impairment to determine if the unrealized losses are other-than-temporary. Factors considered in determining whether a loss is other-than-temporary include the length of time and extent to which fair value has been less than the cost basis, the financial condition of the issuer, and our intent and ability to hold the investment until recovery of its amortized cost basis. We intend, and have the ability, to hold our investments in unrealized loss positions until their amortized cost basis has been recovered. Based on our evaluation, we determined that the unrealized losses were not other-than-temporary as of December 31, 2018.

#### 4. Balance Sheet Details

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

	December 31,	
	2018	2017
Computer and office equipment	\$ 543	\$ 425
Scientific and laboratory equipment	5,631	5,494
Tenant improvements	1,703	1,706
	7,877	7,625
Less accumulated depreciation and amortization	(6,024)	(5,345)
	<u>\$ 1,853</u>	<u>\$ 2,280</u>

As of December 31, 2018, 2017 and 2016, depreciation expense was \$0.7 million, \$0.7 million and \$0.9 million, respectively.

Accrued expenses consist of the following (in thousands):

	December 31,	
	2018	2017
Accrued salaries, wages and benefits	\$ 1,309	\$ 1,920
Other accrued expenses (1)	717	1,183
	<u>\$ 2,026</u>	<u>\$ 3,103</u>

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

#### 5. Debt, Commitments and Contingencies

##### Term Loans

In November 2016, we entered into a loan and security agreement 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 enables the Lenders to require immediate repayment of the outstanding debt. The material adverse change clause covers a material impairment in the perfection or priority of the lenders' lien in the underlying collateral or in the value of such collateral, material adverse change in business operations or condition or material impairment of our prospects for repayment of any portion of the remaining debt obligation.

As of December 31, 2018, the carrying value of our Term Loans consists of \$15.3 million principal outstanding, less the debt issuance costs of \$0.3 million. 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.

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

	<u>December 31,</u> <u>2018</u>	<u>December 31,</u> <u>2017</u>
Debt balance	\$ 15,333	\$ 20,000
Less debt issuance costs and discount	(115)	(345)
Long-term debt, net of issuance costs and discount	15,218	19,655
Less current portion of long-term debt	(8,000)	(5,333)
Add accrual of final payment	1,045	397
Long-term debt, net of current portion and issuance costs and discount	<u>\$ 8,263</u>	<u>\$ 14,719</u>
Current portion of long-term debt	\$ 8,000	\$ 5,333
Less current portion of debt issuance costs and discount	(233)	(321)
Current portion of long-term debt, net of issuance costs and discount	<u>\$ 7,767</u>	<u>\$ 5,012</u>

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

	<u>December 31, 2018</u>
2019	\$ 8,000
2020	7,333
	<u>\$ 15,333</u>

The final maturity payment of \$1.8 million is accruing over the life of the Term Loans through interest expense.

#### Facility Lease

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. In July 2018, we entered into a lease amendment that reduced the space we lease from 24,494 square feet to 20,508 square feet and extended the lease term to May 2023.

Rent expense for the years ended December 31, 2018, 2017 and 2016 was \$1.0 million, \$0.9 million and \$0.5 million, respectively.

As of December 31, 2018, future minimum payments under the non-cancelable operating lease are as follows (in thousands):

	<b>Operating Lease</b>
2019	\$ 812
2020	1,002
2021	1,031
2022	1,062
Thereafter	403
	<u>\$ 4,310</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. In May 2018, we provided TSRI with written notice of termination of our research funding and option agreement effective as of November 2018. During the years ended December 31, 2018, 2017 and 2016, we recognized expense under the agreement in the amount of \$1.7 million, \$1.8 million and \$1.6 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.

### Strategic Advisor Agreement

In November 2017, John D. Mendlein, Ph.D., a member of our Board of Directors since July 2010 and our Chief Executive Officer from September 2011 to November 2017, began serving as a strategic advisor to us pursuant to the terms of a strategic advisor agreement entered with Dr. Mendlein on November 1, 2017 (Strategic Advisor Agreement). Pursuant to the terms of the Strategic Advisor Agreement, we agreed to, among other things, pay Dr. Mendlein as a strategic advisor to us for a period of up to four years, at a monthly rate of \$42,500 for the first year and \$7,500 per month for the rest of the term. Either party may terminate the Strategic Advisor Agreement after the first year, provided that payments under the Strategic Advisor Agreement and continued vesting of outstanding employee stock options are guaranteed through the second year of the Strategic Advisor Agreement in the event the Board terminates the Strategic Advisor Agreement for convenience or Dr. Mendlein terminates for our material breach of the Strategic Advisor Agreement. For the year ended December 31, 2018, we recognized expenses under the Strategic Advisor Agreement in the amount of \$0.5 million.

## 6. Stockholders' Equity

### Common Stock

#### 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, par value \$0.001 per share, at a price of \$37.10 per share, 2,285,952 shares of our Class X Convertible Preferred Stock (Preferred Stock, and together with the common stock, the Shares), par value \$0.001 per share, at a price of \$13.25 per share, and warrants to purchase up to that number of additional shares of common stock equal to thirty seven and one half percent (37.5%) of the number of Shares purchased by VGO Fund on an if-converted to common stock basis (rounded up to the nearest whole share), and the remaining Purchasers purchased an aggregate of 292,453 shares of our common stocks, at a price of \$37.10 per share, and warrants to purchase up to that number of additional shares of common stock equal to thirty-seven and one half percent (37.5%) of the number of common stocks purchased by such Purchaser (rounded up to the nearest whole share). Gross proceeds from the private placement were \$45.8 million. After giving effect to costs related to the private placement, net proceeds were \$42.5 million.

Each share of Preferred Stock is convertible into 0.357 shares of our common stock. VGO Fund is prohibited from converting the Preferred Stock into shares of our common stock if, as a result of such conversion, VGO Fund, together with its affiliates, would own more than 9.50% of the shares of our common stock then issued and outstanding, which percentage may change at VGO Fund's election upon 61 days' notice to us.

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

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

We evaluated the Preferred Stock for liability or equity classification under ASC 480, *Distinguishing Liabilities from Equity* (ASC480), and determined that equity treatment was appropriate because the Preferred Stock did not meet the definition of the liability instruments defined thereunder for convertible instruments. Specifically, the Preferred Stock are not mandatorily redeemable and do not embody an obligation to buy back the shares outside of our control in a manner that could require the transfer of assets. Additionally, we determined that the Preferred Stock would be recorded as permanent equity, not temporary equity, based on the guidance of ASC 480 given that they are not redeemable for cash or other assets (i) on a fixed or determinable date, (ii) at the option of the holder, and (iii) upon the occurrence of an event that is not solely within control of the Company.

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

The issuance of convertible preferred stock could generate a beneficial conversion feature (BCF), which arises when a debt or equity security is issued with an embedded conversion option that is beneficial to the investor (or in-the-money) at inception because the conversion option has an effective strike price that is less than the market price of the underlying stock on the commitment date. The fair value of our common stock at the commitment date in August 2017 was \$33.18, using the Black-Scholes valuation model. After the proceeds allocation, the Preferred Stock have an effective conversion price of \$33.18 per common share, which was equal to the fair value of our common stock on the commitment date. Therefore, no BCF is present.

The warrants are exercisable at an exercise price of \$64.92 per share, subject to adjustments as provided under the terms of the warrants. The warrants are immediately exercisable and expire on December 31, 2019. We also entered into a registration rights agreement (Registration Rights Agreement) with certain of the Purchasers, excluding those Purchasers affiliated with our directors and officers, requiring us to register for the resale of the relevant securities. We registered all of the relevant securities issued in the private placement for resale on a Form S-3 filed with the SEC, as required under the Registration Rights Agreement, and the registration statement was declared effective in September 2017.

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

### **Registration Statement on Form S-3**

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

In October 2018, we started utilizing the ATM Offering Program and sold an aggregate of 49,723 shares of common stock at an average price of \$9.92 per common share for net proceeds of \$0.4 million through December 31, 2018.

### **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. Total shares available for issuance under the 2015 Plan as of January 1, 2019 were 194,614. 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 September 2016, we granted a non-qualified option to purchase 10,357 shares of our common stock at an exercise price of \$46.06 per share as an inducement award in connection with the hiring of our Senior Vice President, Research (who was later promoted to Chief Scientific Officer) and filed a registration statement on Form S-8 on March 22, 2017 to register shares of common stock underlying this option. Upon resignation of our Chief Scientific Officer effective December 31, 2018, any unvested shares underlying this option were cancelled. Vested shares were exercisable within 90 days from termination date.

We did not grant an inducement non-qualified option in 2017.

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). We intend to file a registration statement on Form S-8 to register the shares of common stock underlying the options granted in July 2018 prior to the time at which this option becomes exercisable. In addition, from time to time, we may make inducement grants of stock options to new employees.

## **Employee Stock Purchase Plan**

In April 2015, our board of directors adopted, and our stockholders approved, our 2015 Employee Stock Purchase Plan (the 2015 ESPP). The 2015 ESPP became effective on May 6, 2015. A total of 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, 2019, total shares reserved for issuance under the 2015 ESPP were 81,778.



## 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, 2017	329,634	\$ 77.24		
Granted	149,325	\$ 32.84		
Exercised	(864)	\$ 15.43		
Canceled/forfeited/expired	(121,742)	\$ 66.04		
Outstanding as of December 31, 2018	<u>356,353</u>	<u>\$ 62.61</u>	<u>6.97</u>	<u>\$ 427</u>
Options vested and expected to vest as of December 31, 2018	<u>356,353</u>	<u>\$ 62.61</u>	<u>6.97</u>	<u>\$ 427</u>
Options exercisable as of December 31, 2018	<u>203,974</u>	<u>\$ 77.24</u>	<u>5.62</u>	<u>\$ 427</u>

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,		
	2018	2017	2016
Expected term (in years)	5.00 – 6.08	5.50 – 6.08	5.50 – 6.08
Risk-free interest rate	2.3% – 3.0%	1.9% – 2.1%	1.2% – 2.1%
Expected volatility	87.9% – 98.4%	99.1% – 124.4%	80.7% – 84.5%
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,		
	2018	2017	2016
Expected term (in years)	0.50	0.50	0.50
Risk-free interest rate	1.4% – 2.1%	0.6% – 1.0%	0.4% – 0.6%
Expected volatility	71.5% – 99.7%	74.5% – 115.2%	75.5% – 80.8%
Expected dividend yield	0.0%	0.0%	0.0%

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

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

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

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

### **Performance Options with Market Conditions**

In October 2015, we granted to our executives, employees and certain consultants performance options with a market condition to purchase up to an aggregate 12,100 shares of common stock at an exercise price of \$143.36. Upon achievement of specified market condition by October 2017, such performance options shall begin to vest over four years in equal monthly installments, otherwise the options will be subject to forfeiture. The fair value of the performance options with market conditions is estimated on the date of the grant using a Monte Carlo simulation, based on the market price of the underlying common stock, expected performance measurement period, expected peer group stock price volatility and expected risk-free interest rate. The weighted average grant date fair value was \$59.22. The performance options with market conditions grants are expensed using the accelerated attribution method over the requisite service period of 4.8 years regardless of whether the market condition is achieved or earned and vested. As of October 2017, the market condition for these performance options were not met and therefore were forfeited.

In January 2016, we granted to our executives, employees and certain consultants performance options with a market condition to purchase up to an aggregate 28,354 shares of common stock at an exercise price of \$127.82. Upon achievement of specified market conditions by January 2018, such performance options shall begin to vest over four years in equal monthly installments, otherwise the options will be subject to forfeiture. The fair value of the performance options with a market condition is estimated on the date of the grant using a Monte Carlo simulation, based on the market price of the underlying common stock, expected performance measurement period, expected peer group stock price volatility and expected risk-free interest rate. The weighted average grant date fair value was \$27.02. The performance options with market conditions grants are expensed using the accelerated attribution method over the requisite service period of 5.1 years regardless of whether the market condition is achieved or earned and vested. As of January 2018, the market condition for these performance options were not met and therefore were forfeited.

There were no performance options with a market condition granted during 2017 and 2018.

### **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, 2017	3,520	\$ 59.95
Granted	19,294	\$ 11.91
Released	(2,806)	\$ 63.45
Forfeited	(4,538)	\$ 17.31
Balance as of December 31, 2018	<u>15,470</u>	<u>\$ 11.91</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>Twelve Months Ended December 31,</b>		
	<b>2018</b>	<b>2017</b>	<b>2016</b>
Research and development	\$ 1,216	\$ 1,399	\$ 1,876
General and administrative	2,215	5,385	3,153
Total share-based compensation expense	<u>\$ 3,431</u>	<u>\$ 6,784</u>	<u>\$ 5,029</u>

The weighted-average grant date fair value per share of stock options granted by us, excluding performance options with market conditions, during the years ended December 31, 2018, 2017 and 2016 was \$25.76, \$39.90 and \$46.76, respectively. The total grant date fair value of restricted stock units vested during the years ended December 31, 2018, 2017 and 2016 was \$0.2 million, \$0.1 million and \$13,000, respectively. The aggregate intrinsic value of stock options exercised during the years ended December 31, 2018, 2017 and 2016 was \$6,000, \$0.3 million and \$34,000, respectively. The aggregate intrinsic value of restricted stock units released during the years ended December 31, 2018, 2017 and 2016 was \$19,000, \$0.1 million and \$4,000. As of December 31, 2018, total unrecognized share-based compensation expense related to unvested stock options and restricted stock units was approximately \$3.9 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 2.6 years and 1.4 years, respectively.

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

### Warrants

Warrants outstanding as of December 31, 2018 are as follows:

Number Outstanding	Exercise Price Per Share	Expiration Date
463,735	\$ 64.92	December 2019
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>477,639</u>		

### Common Stock Reserved for Future Issuance

Common stock reserved for future issuance is as follows:

	Years Ended December 31,	
	2018	2017
Class X Preferred Stock (if-converted to common stock)	816,851	816,851
Common stock warrants	477,639	477,639
Common stock options and awards outstanding	371,823	333,154
Shares available under the 2015 Plan	107,246	54,720
Shares available under the 2015 ESPP	59,936	41,687
	<u>1,833,495</u>	<u>1,724,051</u>

## 7. Income Tax

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

	Years Ended December 31,		
	2018	2017	2016
United States	\$ (34,021)	\$ (47,712)	\$ (57,096)
Foreign	(494)	(495)	(808)
	<u>\$ (34,515)</u>	<u>\$ (48,207)</u>	<u>\$ (57,904)</u>

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

	Years Ended December 31, (1)		
	2018	2017	2016
Expected income taxes benefit at federal statutory rate	\$ (7,248)	\$ (16,390)	\$ (19,687)
State income taxes, net of federal benefit	(14)	(13)	—
Permanent items and other	770	1,311	675
Research credits	(1,222)	(2,286)	(6,800)
Unrecognized tax benefits	489	914	2,720
Foreign rate differential	22	87	141
Change in tax rate	(11)	(25)	—
Tax cuts and Jobs Act	—	27,933	—
Change in valuation allowance	7,214	(11,531)	22,902
Income tax (benefit) expense	<u>\$ —</u>	<u>\$ —</u>	<u>\$ (49)</u>

(1) For the years ended December 31, 2017 and 2016, the statutory tax rate was 34%. For the year ended December 31, 2018, as a result of the TJCA, the statutory tax rate was decreased to 21%.

The TJCA was enacted on December 22, 2017. The TJCA reduces the US federal corporate tax rate from 35 percent to 21 percent, requires companies to pay a one-time transition tax on earnings of certain foreign subsidiaries that were previously tax deferred, and creates new taxes on certain foreign sourced earnings. At December 31, 2017, we made a reasonable estimate of the effects on their existing deferred tax balances. At December 31, 2017, we recognized a provisional amount of \$27.9 million, which was included as a component of income tax expense from continuing operations offset with valuation allowances. As of December 31, 2018, we had completed our assessment of the impact of the TCJA and has reflected the impact in the current year.

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 \$66.9 million and \$59.7 million as of December 31, 2018 and 2017, 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,	
	2018	2017
Net operating loss carryforwards	\$ 32,997	\$ 27,226
Capitalized research and development expenses	17,279	16,218
Research credits and other state credits	11,962	11,229
Intangible assets	2,024	2,210
Reserve and accruals	2,667	2,843
Valuation allowance	(66,929)	(59,726)
Net deferred tax assets	<u>\$ —</u>	<u>\$ —</u>

As of December 31, 2018, we had federal net operating loss carryforwards of approximately \$139.5 million, with \$27.0 million of net operating losses generated after December 31, 2017 carrying forward indefinitely and \$112.5 million of net operating losses that will begin to expire in 2025. We had state net operating loss carryforwards of approximately \$148.2 million, and foreign net operating loss carryforwards of \$7.5 million. The state net operating losses will begin to expire in 2021. The foreign net operating losses carry over indefinitely.

As of December 31, 2018, we had federal and state research and development credit carryforwards of approximately \$4.4 million and \$3.8 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, 2018, 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 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, 2018, 2017 and 2016.

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.

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

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

	<b>December 31,</b>		
	<b>2018</b>	<b>2017</b>	<b>2016</b>
Balance as of beginning of year	\$ 16,558	\$ 13,000	\$ 5,033
Increase (decrease) related to prior year tax positions	2	(189)	1,890
Increase related to current year tax positions	3,083	3,747	6,077
Balance as of end of year	<u>\$ 19,643</u>	<u>\$ 16,558</u>	<u>\$ 13,000</u>

We do not anticipate that the amount of unrecognized tax benefits as of December 31, 2018 will change within the next twelve months.

## 8. Employee Benefits

### 401(k) Plan

We maintain a defined contribution 401(k) plan available to eligible employees. Employee contributions are voluntary and are determined on an individual basis, limited to the maximum amount allowable under federal tax regulations. In April 2015, our Board of Directors approved a policy, beginning on June 1, 2015, to match employee contributions equal to 50% of the participant's contribution of up to a maximum of 6% of the participant's annual salary. We made discretionary contributions totaling \$0.2 million during each of the years ended December 31, 2018, 2017 and 2016, respectively.

## 9. Quarterly Financial Data (Unaudited)

The following financial information reflects all normal recurring adjustments, which are, in our opinion, necessary for a fair statement of the results of the interim periods. Summarized quarterly data for 2018 and 2017 are as follows (in thousands, except per share data):

	For the Quarters Ended			
	March 31	June 30	September 30	December 31
<b>2018:</b>				
Operating expenses	\$ 10,220	\$ 9,960	\$ 6,677	\$ 5,963
Net loss	(10,667)	(10,412)	(7,114)	(6,322)
Basic and diluted net loss per share	\$ (5.01)	\$ (4.88)	\$ (3.33)	(2.92)
<b>2017:</b>				
Operating expenses	\$ 13,211	\$ 11,907	\$ 10,827	\$ 11,200
Net loss	(13,405)	(12,138)	(11,190)	(11,474)
Basic and diluted net loss per share	\$ (7.90)	\$ (7.13)	\$ (6.06)	(5.39)

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

## 10. Subsequent Events

In January 2019, the VGO Fund converted 641,991 shares of its Preferred Stock into 229,283 shares of common stock. After the conversion, VGO Fund owns 9.50% of our common stock.

In March 2019, we entered into a research collaboration and option agreement with CSL Behring for the development of product candidates derived from up to four tRNA synthetases from our preclinical pipeline. Under the terms of the collaboration, CSL Behring will fund all research and development activities related to the development of the applicable product candidates for the duration of the collaboration. CSL Behring will 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 achievement of research milestones and CSL Behring's determination to continue development. In addition, aTyr will grant CSL Behring 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.

As of March 22, 2019, we issued and sold 184,346 shares of common stock at a weighted average price of \$7.34 per share through our ATM Offering Program and received total net proceeds of \$1.3 million.

## 11. Event (Unaudited) Subsequent to the Date of the Independent Auditor's Report

On December 31, 2019, 463,735 warrants to purchase our common stock issued in August 2017 to investors who participated in our private placement offering, expired pursuant to the terms of the warrant agreement.

On January 6, 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.

On January 7, 2020, the VGO Fund converted 1,142,478 shares of its Preferred Stock into 408,247 shares of common stock. After the conversion, VGO Fund owns 9.50% of our common stock.

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

	September 30, 2019 (unaudited)	December 31, 2018
<b>Assets</b>		
Current assets:		
Cash and cash equivalents	\$ 17,341	\$ 22,962
Available-for-sale investments, short-term	20,723	26,583
Prepaid expenses and other assets	1,080	1,258
Total current assets	39,144	50,803
Property and equipment, net	1,386	1,853
Right-of-use assets	2,994	—
Other assets	221	90
Total assets	\$ 43,745	\$ 52,746
<b>Liabilities and Stockholders' Equity</b>		
Current liabilities:		
Accounts payable	\$ 1,324	\$ 1,040
Accrued expenses	1,579	2,026
Contract liability	352	—
Current portion of operating lease liability	729	—
Current portion of long-term debt, net of issuance costs and discount	7,844	7,767
Total current liabilities	11,828	10,833
Long-term operating lease liability, net of current portion	2,439	—
Long-term debt, net of current portion and issuance costs and discount	2,742	8,263
Commitments and contingencies (Note 4)		
Stockholders' equity:		
Preferred stock, \$0.001 par value; 5,000,000 undesignated authorized shares; Class X Convertible Preferred Stock issued and outstanding shares – 1,643,961 and 2,285,952 as of September 30, 2019 and December 31, 2018, respectively	2	2
Common stock, \$0.001 par value; 10,714,286 authorized shares; issued and outstanding shares – 3,890,185 and 2,186,389 as of September 30, 2019 and December 31, 2018, respectively	50	31
Additional paid-in capital	343,048	332,378
Accumulated other comprehensive loss	(33)	(60)
Accumulated deficit	(316,331)	(298,701)
Total stockholders' equity	26,736	33,650
Total liabilities and stockholders' equity	\$ 43,745	\$ 52,746

*See accompanying notes.*

aTyr Pharma, Inc.

Condensed Consolidated Statements of Operations  
(in thousands, except share and per share data)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2019	2018	2019	2018
	(unaudited)			
Revenues:				
Collaboration revenue	\$ 184	\$ —	\$ 278	\$ —
Total revenues	184	—	278	—
Operating expenses:				
Research and development	3,799	4,202	10,458	16,836
General and administrative	1,883	2,475	6,836	10,021
Total operating expenses	5,682	6,677	17,294	26,857
Loss from operations	(5,498)	(6,677)	(17,016)	(26,857)
Total other income (expense), net	(147)	(437)	(614)	(1,336)
Net loss	\$ (5,645)	\$ (7,114)	\$ (17,630)	\$ (28,193)
Net loss per share attributable to common stock holders, basic and diluted	\$ (1.47)	\$ (3.33)	\$ (5.55)	\$ (13.22)
Weighted average common stock shares outstanding, basic and diluted	3,846,249	2,134,909	3,175,177	2,133,055

See accompanying notes.



aTyr Pharma, Inc.

Condensed Consolidated Statements of Comprehensive Loss  
(in thousands)

	<u>Three Months Ended September 30,</u>		<u>Nine Months Ended September 30,</u>	
	<u>2019</u>	<u>2018</u>	<u>2019</u>	<u>2018</u>
	<b>(unaudited)</b>			
Net loss	\$ (5,645)	\$ (7,114)	\$ (17,630)	\$ (28,193)
Other comprehensive gain (loss):				
Change in unrealized gain (loss) on available-for-sale investments, net of tax	(1)	28	27	63
Comprehensive loss	<u>\$ (5,646)</u>	<u>\$ (7,086)</u>	<u>\$ (17,603)</u>	<u>\$ (28,130)</u>

See accompanying notes.

aTyr Pharma, Inc.

Condensed Consolidated Statements of Stockholders' Equity  
(in thousands, except share data)

Three and Nine Months Ended September 30, 2019 (unaudited)

	Convertible Preferred Stock		Common Stock		Additional Paid-In Capital	Other Comprehensive Gain/(Loss)	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount	Shares	Amount				
Balance as of December 31, 2018	2,285,952	\$ 2	2,186,389	\$ 31	\$ 332,378	\$ (60)	\$ (298,701)	\$ 33,650
Conversion of preferred stock to common stock	(641,991)	—	229,283	3	(3)	—	—	—
Issuance of common stock from at the market offerings, net of offering costs	—	—	193,670	3	1,378	—	—	1,381
Stock-based compensation	—	—	—	—	571	—	—	571
Net unrealized gain on investments, net of tax	—	—	—	—	—	20	—	20
Net loss	—	—	—	—	—	—	(6,137)	(6,137)
Balance as of March 31, 2019	1,643,961	\$ 2	2,609,342	\$ 37	\$ 334,324	\$ (40)	\$ (304,838)	\$ 29,485
Issuance of common stock upon release of restricted stock units	—	—	7,487	—	—	—	—	—
Issuance of common stock pursuant to employee stock purchase plan	—	—	1,515	—	8	—	—	8
Issuance of common stock from at the market offerings, net of offering costs	—	—	252,872	3	1,143	—	—	1,146
Issuance of common stock from registered direct offering, net of offering costs	—	—	660,154	9	4,909	—	—	4,918
Stock-based compensation	—	—	—	—	509	—	—	509
Net unrealized gain on investments, net of tax	—	—	—	—	—	8	—	8
Net loss	—	—	—	—	—	—	(5,848)	(5,848)
Balance as of June 30, 2019	1,643,961	\$ 2	3,531,370	\$ 49	\$ 340,893	\$ (32)	\$ (310,686)	\$ 30,226
Issuance of common stock from at the market offerings, net of offering costs	—	—	358,815	1	1,877	—	—	1,878
Stock-based compensation	—	—	—	—	278	—	—	278
Net unrealized loss on investments, net of tax	—	—	—	—	—	(1)	—	(1)
Net loss	—	—	—	—	—	—	(5,645)	(5,645)
Balance as of September 30, 2019	1,643,961	\$ 2	3,890,185	\$ 50	\$ 343,048	\$ (33)	\$ (316,331)	\$ 26,736

Three and Nine Months Ended September 30, 2018 (unaudited)

	Convertible Preferred Stock		Common Stock		Additional Paid-In Capital	Other Comprehensive Gain/(Loss)	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount	Shares	Amount				
Balance as of December 31, 2017	2,285,952	\$ 2	2,129,968	\$ 30	\$ 328,519	\$ (120)	\$ (264,186)	\$ 64,245
Issuance of common stock upon exercise of options and release of restricted stock units	—	—	2,823	—	8	—	—	8
Stock-based compensation	—	—	—	—	928	—	—	928
Net unrealized loss on investments, net of tax	—	—	—	—	—	(16)	—	(16)
Net loss	—	—	—	—	—	—	(10,667)	(10,667)
Balance as of March 31, 2018	2,285,952	\$ 2	2,132,791	\$ 30	\$ 329,455	\$ (136)	\$ (274,853)	\$ 54,498
Issuance of common stock upon exercise of options and release of restricted stock units	—	—	238	—	—	—	—	—
Issuance of common stock pursuant to employee stock purchase plan	—	—	1,778	—	28	—	—	28
Stock-based compensation	—	—	—	—	1,211	—	—	1,211
Net unrealized gain on investments, net of tax	—	—	—	—	—	51	—	51
Net loss	—	—	—	—	—	—	(10,412)	(10,412)
Balance as of June 30, 2018	2,285,952	\$ 2	2,134,807	\$ 30	\$ 330,694	\$ (85)	\$ (285,265)	\$ 45,376
Issuance of common stock upon exercise of options and release of restricted stock units	—	—	609	—	6	—	—	6
Stock-based compensation	—	—	—	—	690	—	—	690
Net unrealized gain on investments, net of tax	—	—	—	—	—	28	—	28
Net loss	—	—	—	—	—	—	(7,114)	(7,114)
Balance as of September 30, 2018	2,285,952	\$ 2	2,135,416	\$ 30	\$ 331,390	\$ (57)	\$ (292,379)	\$ 38,986

See accompanying notes.

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

	<b>Nine Months Ended September 30,</b>	
	<b>2019</b>	<b>2018</b>
	<b>(unaudited)</b>	
<b>Cash flows from operating activities:</b>		
Net loss	\$ (17,630)	\$ (28,193)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	478	567
Stock-based compensation	1,358	2,829
Debt discount accretion and non-cash interest expense	556	743
Accretion of discount of available-for-sale investment securities	(245)	(213)
Amortization of right-of-use assets	536	—
Gain on disposal of property and equipment	(28)	—
Changes in operating assets and liabilities		
Prepaid expenses and other assets	9	182
Accounts payable and accrued expenses	(159)	(2,139)
Contract liability	352	—
Operating lease liability	(324)	—
Net cash used in operating activities	(15,097)	(26,224)
<b>Cash flows from investing activities:</b>		
Purchases of property and equipment	(38)	(585)
Purchases of available-for-sale investment securities	(34,668)	(23,375)
Maturities of available-for-sale investment securities	40,800	63,265
Proceeds from sale of property and equipment	51	—
Net cash provided by investing activities	6,145	39,305
<b>Cash flows from financing activities:</b>		
Proceeds from issuance of common stock through employee stock purchase plan	8	28
Proceeds from issuance of common stock through option exercises and release of restricted stock units	—	14
Proceeds from issuance of common stock through at the market offerings, net of offering costs	4,405	—
Proceeds from issuance of common stock through registered direct offering, net of offering costs	4,918	—
Repayments on borrowings	(6,000)	(2,667)
Net cash provided by (used in) financing activities	3,331	(2,625)
Net change in cash and cash equivalents	(5,621)	10,456
Cash and cash equivalents at beginning of period	22,962	21,091
Cash and cash equivalents at the end of period	\$ 17,341	\$ 31,547

*See accompanying notes.*

**Notes to Condensed Consolidated Financial Statements  
(Unaudited)**

**1. Organization, Business, Basis of Presentation and Summary of Significant Accounting Policies**

**Organization and Business**

aTyr Pharma, Inc. (we, us, and our) was 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 condensed 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.

**Unaudited Interim Financial Information**

The accompanying interim condensed consolidated financial statements are unaudited. These unaudited interim financial statements have been prepared in accordance with United States generally accepted accounting principles (GAAP) and follow the requirements of the United States Securities and Exchange Commission (SEC) for interim reporting. As permitted under those rules, certain footnotes or other financial information that are normally required by GAAP can be condensed or omitted. In our opinion, the unaudited interim financial statements have been prepared on the same basis as the audited financial statements and include all adjustments, which include only normal recurring adjustments, necessary for the fair presentation of our financial position and our results of operations and cash flows for periods presented. These statements do not include all disclosures required by GAAP and should be read in conjunction with our financial statements and accompanying notes for the fiscal year ended December 31, 2018, contained in our Annual Report on Form 10-K filed with the SEC on March 26, 2019. The results of the interim periods are not necessarily indicative of the results expected for the full fiscal year or any other interim period or any future year or period.

**Reverse Stock Split**

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. The accompanying condensed consolidated financial statements and notes thereto 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 condensed 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 September 30, 2019, we had an accumulated deficit of \$316.3 million and we expect to continue to incur net losses for the foreseeable future. We believe that our existing cash, cash equivalents and available-for-sale investments of \$38.1 million as of September 30, 2019, will be sufficient to meet our anticipated cash requirements for a period of at least one year from the date of this prospectus.

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 other arrangements when needed on favorable terms or at all. Our failure to raise capital or enter into such other arrangements when needed would have a negative impact on our financial condition and ability to develop our product candidates.

## Use of Estimates

Our condensed consolidated financial statements are prepared in accordance with GAAP. The preparation of our condensed consolidated financial statements requires us to make estimates and assumptions that impact the reported amounts of assets, liabilities, revenues and expenses and the disclosure of contingent assets and liabilities in our condensed consolidated financial statements and accompanying notes. The most significant estimates in our condensed consolidated financial statements relate to clinical trials and research and development expense accruals. 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.

## 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 condensed 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 condensed 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 condensed 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. 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.

## Net Loss Per Share

Basic net loss per share is calculated by dividing the net loss 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 is calculated by dividing the net loss 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, 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 considered for the calculation of diluted net loss per share are as follows (in common share equivalents):

	<b>Three and Nine Months Ended</b>	
	<b>September 30,</b>	
	<b>2019</b>	<b>2018</b>
Class X Preferred Stock (if-converted to common stock)	587,445	816,851
Common stock warrants	477,639	477,639
Common stock options and restricted stock units	402,538	401,168
Employee stock purchase plan	2,067	1,942
	<u>1,469,689</u>	<u>1,697,600</u>

### Recent Accounting Pronouncements

In February 2016, the Financial Accounting Standards Board (FASB) issued ASU No. 2016-02, to increase transparency and comparability among organizations by requiring recognition of lease assets and lease liabilities on the balance sheet and disclosure of key information about leasing arrangements. The new standard was effective beginning after December 15, 2018, including interim periods within those periods, using a modified retrospective approach. We adopted ASU No. 2016-02 on January 1, 2019 and recognized a \$3.5 million right-of-use asset and \$3.5 million lease liability in our condensed 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 condensed 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 condensed 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 condensed 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. The amendments for ASU No. 2018-18 are effective for fiscal years beginning after December 15, 2019, and interim periods within those fiscal years. Early adoption is permitted, including adoption in any interim period, (1) for public business entities for which financial statements have not yet been issued and (2) for all other entities for periods which financial statements have not yet been made available for issuance. An entity may not adopt the amendments earlier than its adoption date of Topic 606. 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 condensed consolidated financial position or results of operations.

## 2. 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 carrying value of our long-term debt approximates its fair value. Investment securities are recorded at fair value.

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

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

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

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

Financial assets measured at fair value on a recurring basis consist of investment securities. Investment securities are recorded at fair value, defined as the exit price in the principal market in which we would transact, representing the amount that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants. Level 2 securities are valued using quoted market prices for similar instruments, non-binding market prices that are corroborated by observable market data, or discounted cash flow techniques and include our investments in corporate debt securities and commercial paper. 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 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 September 30, 2019</b>				
Assets:				
Current:				
Cash equivalents	\$ 16,016	\$ 16,016	\$ —	\$ —
Available-for-sale investments, short-term:				
Asset-backed securities	4,297	—	4,297	—
Commercial paper	9,357	—	9,357	—
Corporate debt securities	7,069	—	7,069	—
Total short-term investments	20,723	—	20,723	—
Total assets measured at fair value	\$ 36,739	\$ 16,016	\$ 20,723	\$ —

	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 September 30, 2019 and December 31, 2018, available-for-sale investments are detailed as follows (in thousands):

	September 30, 2019			
	Gross Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Market Value
Available-for-sale investments, short-term:				
Asset-backed securities	\$ 4,292	\$ 5	\$ —	\$ 4,297
Commercial paper	9,357	—	—	9,357
Corporate debt securities	7,057	12	—	7,069
	\$ 20,706	\$ 17	\$ —	\$ 20,723



	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>

As of September 30, 2019, all of our available-for-sale investments had a variety of effective maturity dates of less than one year. As of September 30, 2019, all available-for-sale investments were in gross unrealized gain positions.

At each reporting date, we perform an evaluation of impairment to determine if any unrealized losses are other-than-temporary. Factors considered in determining whether a loss is other-than-temporary include the length of time and extent to which fair value has been less than the cost basis, the financial condition of the issuer, and our intent and ability to hold the investment until recovery of its amortized cost basis. We intend, and have the ability, to hold our investments in unrealized loss positions, if any, until their amortized cost basis has been recovered.

### 3. Research Collaboration

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 (\$17.0 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 September 30, 2019, no research milestone 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 their 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 three and nine months ended September 30, 2019, we recognized \$184,000 and \$278,000 respectively, as collaboration revenue under the CSL Agreement.

#### 4. 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 and Solar Capital Ltd. (the 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.

Under the Loan Agreement, we were obligated to make interest only payments through June 1, 2018. Beginning June 2018, we were obligated to make consecutive equal monthly payments of principal and interest in arrears through the maturity date of November 18, 2020. 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.

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

As of September 30, 2019, the carrying value of our Term Loans consisted of \$9.3 million principal outstanding and a \$1.4 million accretion of the final payment less the debt issuance costs of \$0.2 million. The final payment of \$1.8 million is accruing over the life of the Term Loans through interest expense and is due in the fourth quarter of 2020. The debt issuance costs have been recorded as a debt discount which are being accreted to interest expense over the life of the Term Loans.

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. 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 a debt discount which is being accreted to interest expense over the life of Term Loans.

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

	<b>September 30, 2019</b>
Debt balance	\$ 9,333
Less debt issuance costs and discount	(8)
Long-term debt, net of issuance costs and discount	9,325
Less current portion of long-term debt	(8,000)
Add accrual of final payment	1,417
Long-term debt, net of current portion and issuance costs and discount	\$ 2,742
Current portion of long-term debt	\$ 8,000
Less current portion of debt issuance costs and discount	(156)
Current portion of long-term debt, net of issuance costs and discount	\$ 7,844

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

	<b>September 30, 2019</b>
2019	\$ 2,000
2020	7,333
Principal payments balance	<u>\$ 9,333</u>

## Leases

We adopted ASU No. 2016-02, utilizing the modified retrospective transition method on January 1, 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 condensed consolidated balance sheets, but did not have a material impact on the condensed consolidated statements of operations. The impact on the condensed 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 also have an immaterial amount of prepaid financing leases that are included within other assets in our condensed consolidated balance sheets. We utilize a discount rate (incremental borrowing rate) of 9.60%. For the three and nine months ended September 30, 2019, we recorded an operating lease cost of \$0.2 million and \$0.7 million, respectively. For the three and nine months ended September 30, 2018, we recorded an operating lease cost of \$0.3 million and \$0.8 million, respectively. As of September 30, 2019, the weighted average remaining lease term was 3.7 years and the weighted average discount rate was 9.6%.

We have a non-cancelable facility lease that is subject to base lease payments, which escalate over the term of the lease, additional charges for common area maintenance and other costs. In July 2018, we entered into a lease amendment that reduced the space we lease from 24,494 square feet to 20,508 square feet and extended the lease term to May 2023. With the lease amendment, we do not have an option to extend the lease.

Future minimum payments under the non-cancelable facility lease and reconciliation to the operating lease liability as of September 30, 2019 were as follows (in thousands):

	<b>Operating Lease</b>
2019	\$ 247
2020	1,002
2021	1,031
2022	1,062
Thereafter	404
Less: Amount representing interest	(578)
Present value of lease payments	<u>3,168</u>
Less: Current portion of operating lease liability	(729)
Long-term operating lease liability	<u>\$ 2,439</u>

## Related Party Transactions

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. For the three and nine months ended September 30, 2018, we recognized expense under the agreement in the amount \$0.5 million and \$1.5 million, respectively. Paul Schimmel, Ph.D., a member of our board of directors, is a faculty member at TSRI and such payments funded a portion of his research activities conducted at TSRI.

## 5. Stockholders' Equity

### 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 nine months ended September 30, 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, at a price of \$13.25 per share, and warrants to purchase up to 353,992 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 are immediately exercisable and expire 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.

#### Common Stock Reserved for Future Issuance

Pursuant to the automatic increase provisions of our 2015 Stock Option and Incentive Plan (2015 Plan) and 2015 Employee Stock Purchase Plan (2015 ESPP), 87,368 additional shares were reserved for future issuance under the 2015 Plan on January 1, 2019 and 21,842 additional shares were reserved for future issuances under the 2015 ESPP on January 1, 2019. At our 2019 Annual Meeting of Stockholders, our stockholders approved an amendment to our 2015 Plan to increase the number of common stock reserved for issuance under the 2015 Plan by 71,428 shares. Common stock reserved for future issuance is as follows:

	<u>September 30, 2019</u>
Class X Preferred Stock (if-converted to common stock)	587,445
Common stock warrants	477,639
Common stock options and restricted stock units	402,538
Shares available under the 2015 Plan	222,014
Shares available under the 2015 ESPP	80,299
	<u>1,769,935</u>

The following table summarizes our stock option activity under all equity incentive plans for the nine months ended September 30, 2019:

	<u>Number of Outstanding Options</u>	<u>Weighted Average Exercise Price</u>
Outstanding as of December 31, 2018	356,353	\$ 62.61
Granted	76,472	\$ 7.17
Canceled/forfeited/expired	(43,119)	\$ 66.09
Outstanding as of September 30, 2019	<u>389,706</u>	\$ 51.35

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

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2019	2018	2019	2018
Expected term (in years)	5.98 – 6.04	6.02 – 6.08	5.51 – 6.07	5.50 – 6.08
Risk-free interest rate	1.4%	2.9%	1.4% – 2.6%	2.3% – 3.0%
Expected volatility	100.7% – 101.0%	88.4% – 88.9%	97.2% – 101.0%	88.4% – 98.4%
Expected dividend yield	0.0%	0.0%	0.0%	0.0%

The following table summarizes our restricted stock unit activity under all equity incentive plans for the nine months ended September 30, 2019:

	Number of Outstanding Restricted Stock Units	Weighted Average Grant Date Fair Value
Balance as of December 31, 2018	15,470	\$ 11.91
Granted	5,356	\$ 7.24
Released	(7,487)	\$ 11.91
Forfeited	(507)	\$ 11.90
Balance as of September 30, 2019	12,832	\$ 9.96

### Stock-based Compensation

The allocation of stock-based compensation for all options, 2015 ESPP purchase rights and restricted stock units is as follows (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2019	2018	2019	2018
Research and development	\$ 82	\$ 204	\$ 285	\$ 1,064
General and administrative	196	486	1,073	1,765
Total stock-based compensation expense	\$ 278	\$ 690	\$ 1,358	\$ 2,829



**4,235,294 Shares of Common Stock**

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**PROSPECTUS**

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*Sole Book-Running Manager*

**Oppenheimer & Co.**

*Lead Manager*

**Roth Capital Partners**

**February 5, 2020**