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Filed Pursuant to Rule 424(b)(4)
Registration No. 333-203272

Prospectus

5,360,000 Shares

Common Stock

This is the initial public offering of shares of common stock of aTyr Pharma, Inc. We are offering 5,360,000 shares in this offering. Prior to this offering, there has been no public market for our common stock. The initial public offering price of our common stock is $14.00 per share. Our common stock has been approved for listing on The NASDAQ Global Select Market under the symbol "LIFE."

We are an "emerging growth company" under applicable Securities and Exchange Commission rules and will be subject to reduced public company reporting requirements.

	Per share	Total
Initial public offering price	$ 14.00	$75,040,000
Underwriting discounts and commissions (1)	$ 0.98	$ 5,252,800
Proceeds to aTyr, before expenses	$ 13.02	$69,787,200

(1) See "Underwriting" for additional disclosure regarding underwriting discounts, commissions and estimated offering expenses.

The underwriters may also purchase up to an additional 804,000 shares from us at the public offering price, less the underwriting discount, within 30 days from the date of this prospectus to cover over-allotments.

Certain of our existing stockholders, including a stockholder affiliated with one of our directors, have indicated an interest in purchasing and have agreed to purchase an aggregate of 1,070,000 shares of our common stock in this offering at the initial public offering price. The underwriting discount for the shares sold to these investors in the offering will be the same as the underwriting discount for the shares sold to the public.

Investing in our common stock involves a high degree of risk. See "Risk Factors" beginning on page 12.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The underwriters expect to deliver the shares on or about May 12, 2015.

J.P. Morgan **Citigroup**

BMO Capital Markets

William Blair

May 6, 2015

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Neither we nor the underwriters have authorized anyone to provide you with information different from that contained in this prospectus or any free writing prospectus. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We and the underwriters are offering to sell, and seeking offers to buy, common stock only in jurisdictions where offers and sales are permitted. The information contained in this prospectus is accurate only as of the date on the front cover page of this prospectus, or other earlier date stated in this prospectus, regardless of the time of delivery of this prospectus or of any sale of our common stock.

The market data and certain other statistical information used throughout this prospectus are based on independent industry publications, governmental publications, reports by market research firms or other independent sources. Some data are also based on our good faith estimates.

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

PROSPECTUS SUMMARY

This 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 common stock, you should carefully read this entire prospectus, including our consolidated financial statements and the related notes included elsewhere in this prospectus. You should also consider, among other things, the matters described under "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations," in each case appearing elsewhere in this prospectus. Unless otherwise stated, all references to "us," "our," "aTyr," "we," the "Company" and similar designations refer to aTyr Pharma, Inc. and its subsidiary, Pangu BioPharma Limited.

Overview

We engage in the discovery and clinical development of innovative medicines for patients suffering from severe, rare diseases using our knowledge of Physiocrine biology, a newly discovered set of physiological modulators. We have discovered approximately 300 Physiocrines (*physio* for life and *crine* for specific activity), a class of naturally occurring proteins that we believe promote homeostasis, a fundamental process of restoring stressed or diseased tissue to a healthier state. Physiocrines are extracellular signaling regions of tRNA synthetases, an ancient family of enzymes that catalyze a key step in protein synthesis. We believe that Physiocrines have evolved over time to modulate important cellular pathways by interacting with various types of cells, including immune and stem cells. Approximately 100 of these proteins interact with the immune system, which we believe presents a significant therapeutic opportunity to restore affected tissues to a healthier state through natural immuno-modulation mechanisms. We successfully completed a Phase 1 clinical trial of Resolaris, our first development candidate from our discovery engine, and are currently conducting a multi-national exploratory Phase 1b/2 clinical trial of Resolaris in adult patients with facioscapulohumeral muscular dystrophy, or FSHD, a severe, rare genetic myopathy with an immune component, for which there are currently no approved treatments. By leveraging our discovery engine and our knowledge of rare diseases, we aim to build a proprietary pipeline of novel product candidates with the potential to treat severe, rare diseases characterized by immune dysregulation. We plan to independently commercialize our Physiocrine-based therapeutics.

Our scientists were the first to identify the Resokine pathway (*reso* for restoring skeletal muscle health and *kine* for activity related to cytokines), an extracellular pathway in human skeletal muscle tissue associated with activities arising from various Physiocrine regions of the histidine aminoacyl tRNA synthetase, or HARS. We believe the Resokine pathway may play an important role in muscle and lung health. Certain patients with antisynthetase syndrome, a rare auto-immune disease, have antibodies to HARS, which are known as Jo-1 antibodies. These Jo-1 antibody patients often develop two significant clinical manifestations, skeletal inflammatory myopathy and interstitial lung disease, or ILD. We believe that the binding of Jo-1 antibodies, particularly to the immuno-modulatory domain of HARS, or iMod domain, blocks HARS immuno-modulatory functions and results in the muscle and lung disease in these Jo-1 antibody patients.

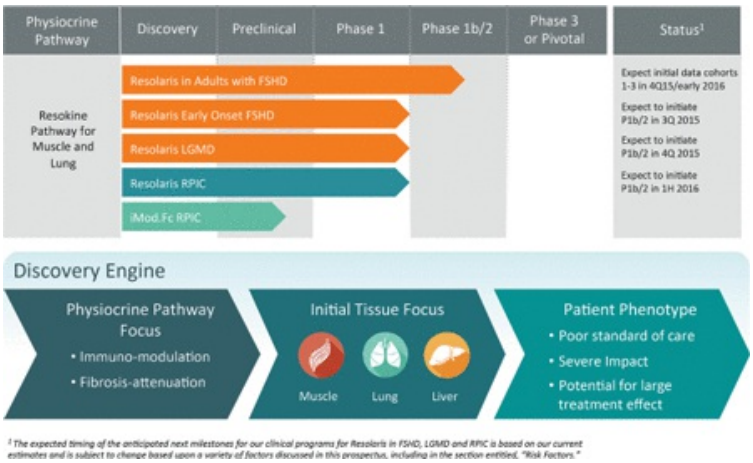
We are harnessing the Resokine pathway and its association with homeostasis in skeletal muscle to develop Resolaris as a first-in-class therapeutic for patients with rare myopathies with an immune component, or RMICs, for which there are limited or no approved treatments. A myopathy is a disease of skeletal muscle tissue, characterized by muscle fiber deterioration, muscle weakness and often an immune response in the affected muscle tissue. In contrast to most current immunology drugs, which are engineered antagonists of immunological pathways, Resolaris is derived from a naturally occurring protein, HARS, which we believe has the potential to reset the immune system in diseased tissue to a more normal state while maintaining the immune system's activity against exogenous, pathogen-based insults. We observed that stimulation of the Resokine pathway through the introduction of Resolaris and its derivatives in rodent models of both severe inflammation and myopathy led to immuno-modulatory effects. We have shown that stimulation of the Resokine pathway by Resolaris alters immune responses and the expression or release of immune-related proteins from cells in response to inflammation. HARS, which

contains the immuno-modulatory domain, is also released from human skeletal muscle. In addition to its immuno-modulatory properties, we believe the Resokine pathway may act on other physiological processes, including processes associated with stem cells, fibrosis and endothelial cells. Our initial therapeutic efforts target severe, rare disease indications in which patients suffer from the immune-related consequences of their genetic disease. We have identified over 20 distinct, molecularly definable RMIC indications, including FSHD and limb-girdle muscular dystrophies, or LGMD, in which we believe Resolaris has the potential to target the immune component of these genetic diseases.

We are also harnessing the Resokine pathway and its potential role in lung disease, specifically ILD, to develop Resolaris as a therapeutic for patients with rare pulmonary diseases with an immune component, or RPICs. ILD is associated with Jo-1 antibody patients and occurs in multiple other clinical settings. We are currently evaluating these other forms of ILD to identify the most appropriate RPIC indication for the initial clinical assessment of augmenting the Resokine pathway with Resolaris.

We have initiated a discovery program to explore varying exposures of the iMod domain of the Resokine pathway through protein engineering. The program seeks to develop a potential therapeutic that we refer to as iMod.Fc. We also believe our proprietary inventory of Physiocrines with their diverse functions have potential therapeutic application in a variety of diseases characterized by tissue dysfunction, including severe diseases of the lung, gut, skin, brain and liver. We intend to leverage our unique understanding of Physiocrines and their functions and our broad intellectual property portfolio, which we believe covers this entire class of potential protein therapeutics, to build a pipeline of product candidates that we expect to develop and commercialize independently for the treatment of various rare diseases.

Below are summaries of our product development pipeline and discovery engine process:



[1] The expected timing of the anticipated next milestones for our clinical programs for Resolaris in FSHD, LGMD and RPIC is based on our current estimates and is subject to change based upon a variety of factors discussed in this prospectus, including in the section entitled, "Risk Factors."

We were founded in 2005 by Paul Schimmel, Ph.D. and Xiang-Lei Yang, Ph.D., two leading aminoacyl tRNA synthetase scientists at The Scripps Research Institute in San Diego, California. Our Executive Chairman and Chief Executive Officer, John D. Mendlein, Ph.D., was formerly the Chief Executive Officer of Adnexus Therapeutics, Inc. (acquired by Bristol-Myers Squibb Company) and Affinium Pharmaceuticals, Ltd. (acquired by Debiopharm Group), and held various roles at Aurora Biosciences Corporation (acquired by Vertex Pharmaceuticals, Incorporated). We have assembled an executive team with broad experience in the discovery, development and commercialization of innovative therapeutics, including transformative therapies for rare genetic diseases, such as Kalydeco, marketed by Vertex Pharmaceuticals Incorporated for the treatment of cystic fibrosis. We are advised by a Therapeutic Advisory Board and a Scientific Advisory Board, both comprised of leaders in the field of biology for medical applications, including our special advisor in immunology, Bruce Beutler, M.D., recipient of the 2011 Nobel Prize in Physiology or Medicine for his work in immunology. Our key investors include entities affiliated with Alta Partners; Cardinal Partners; Domain Associates; Fidelity Management & Research Company; Polaris Partners and Sofinnova Ventures.

Our Physiocrine Advantage: Targeting the Immune System in Genetic Diseases

We believe the immune system is an important component of the pathophysiology of many rare genetic diseases. It is our belief that the immune system acts differently in the presence of some genetic mutations that alter protein levels, structure or function compared to normal tissue. This immune response contributes to a pathophysiologic state in the diseased tissue. By modulating various components of the immune system, Physiocrines can potentially alter this pathophysiological immune activity in the diseased tissue by promoting homeostasis and restoring immune balance in the diseased tissue. Using the immune component as a target or intervention point in the treatment of genetic diseases has precedent as an approach to developing a protein therapeutic. Examples include Soliris, for acquired paroxysmal nocturnal hemoglobinuria (PNH), and Cinryze, for hereditary angioedema (HAE).

Resolaris, Our First Clinical Product Candidate: a Pipeline within a Product Opportunity

Resolaris in FSHD, a Rare Myopathy with an Immune Component (RMIC)

We developed Resolaris based on our discovery of the Resokine pathway in skeletal muscle tissue, an extracellular pathway in human skeletal muscle tissue associated with activities arising from various Physiocrine regions of the human histidine aminoacyl tRNA synthetase. We believe, based on preclinical data and observations from Jo-1 antibody patients, that the Resokine pathway is involved in promoting skeletal muscle health and homeostasis. We believe it does so, in part, by acting as an immunomodulator in skeletal muscle.

Our first clinical development target for Resolaris is FSHD, a rare genetic myopathy in which immune cells invade diseased skeletal muscle and for which there are no approved treatments. The primary clinical phenotype of FSHD is debilitating skeletal muscle deterioration and weakness. The symptoms of FSHD develop in an asymmetrical “muscle by muscle” fashion. This is in contrast to other genetic myopathies, such as Duchenne muscular dystrophy, that usually affect groups of muscles concurrently and symmetrically. In addition to debilitating muscle weakness, FSHD patients often experience severe fatigue, muscle deterioration and pain. The disease is typically diagnosed by the presence of a characteristic pattern of muscle weakness and other clinical symptoms, as well as through genetic testing. While estimates of FSHD prevalence vary, studies exploring the topic have identified average prevalence rates of approximately one in 17,000. Applying this rate to the U.S. population, based on recent census data, yields a domestic FSHD population of approximately 19,000.

We successfully completed a single ascending dose Phase 1 clinical trial in healthy subjects of Resolaris in the first quarter of 2014. Resolaris was found to be well tolerated in all dose cohorts and there were no serious adverse events. We are currently conducting a multi-national exploratory Phase 1b/2 clinical trial of Resolaris in adult patients with FSHD in the European Union. This randomized, double-blind, placebo-controlled trial is

designed to evaluate the safety, tolerability, pharmacokinetics and immunogenicity of multiple intravenous doses of Resolaris in adults with FSHD. We also intend to explore pharmacodynamic changes in immune activity and responses in skeletal muscle. Resolaris is being studied in three dose escalation cohorts (0.3 mg/kg, 1.0 mg/kg and 3.0 mg/kg). In the fourth quarter of 2014, we completed multiple dosing of the patients in the first dose cohort. We recently completed dosing patients in the second cohort and, in April 2015, our independent Data Monitoring Board, or DMB, for the trial recommended that we proceed with the third cohort. We are currently enrolling patients in the third cohort. Subject to our interactions with regulatory authorities and patient enrollment in accordance with our clinical development plans, we expect to report initial results from this clinical trial in the fourth quarter of 2015 or early 2016. In parallel with conducting our initial clinical trial in adults with FSHD, we are finalizing our plans to evaluate Resolaris in a multi-center, international trial of patients with early onset FSHD, which we define as patients with onset of disease before the age of 18. Subject to our interactions with regulatory authorities, we expect to initiate this clinical trial in the third quarter of 2015.

Resolaris in Other RMIC Indications

In addition to FSHD, we plan to address other severe, genetic diseases in which immune cells invade diseased muscle. We are evaluating various forms of limb-girdle muscular dystrophy, or LGMD, a broad class of indications of over 20 rare genetically defined myopathies. These diseases are linked by the common distribution of their muscle weakness (e.g., predominantly in the proximal limb muscles and the pelvic and shoulder girdle muscles). We intend to select genetic forms of LGMD that we believe will be most amenable to treatment with Resolaris, such as those with the characteristics of the associated immuno-pathology in skeletal muscle. We plan to commence clinical trials of Resolaris in at least one LGMD indication in adult patients in the fourth quarter of 2015.

Resolaris Non-Muscle Indication Set: Rare Pulmonary Diseases with an Immune Component (RPICs)

The Resokine pathway may play an important role in lung health. ILD develops in approximately 85% of anti-synthetase syndrome patients with Jo-1 antibodies to Resokine. In addition to its association with Jo-1 antibody patients, ILD occurs in multiple other clinical settings. We are currently evaluating these forms of ILD to identify the most appropriate RPIC indication for the initial clinical assessment of Resolaris. Among these forms of ILD, we have identified several that can result in severe and progressive lung disease and share immuno-pathophysiology features that overlap with our demonstrated Resolaris activities. Examples include idiopathic non-specific interstitial pneumonias, idiopathic pulmonary fibrosis, lymphocytic interstitial pneumonia, bleomycin (the chemotherapeutic agent)-induced pulmonary fibrosis, and ILD in the setting of systemic sclerosis, or scleroderma, and sarcoidosis.

To test that augmenting the Resokine pathway has therapeutic potential in ILD, we have recently generated data in a mouse model of lung inflammation and pulmonary fibrosis induced by bleomycin. The mouse equivalent of Resolaris has shown promising therapeutic activity in this model which has been used previously in the development of therapeutics for different forms of ILD, including the drug pirfenidone or Esbriet, which was approved by the FDA in October 2014 for the treatment of idiopathic pulmonary fibrosis. We noted that Resolaris administration attenuated the radiographic and histological manifestations of pathophysiology in this model when it was dosed therapeutically. These mouse Resolaris pharmacology data provide pre-clinical evidence supporting the therapeutic potential of Resolaris for the treatment of ILD.

We are currently evaluating the most appropriate RPIC indication for the initial clinical evaluation of augmenting the Resokine pathway in lung via Resolaris. The data obtained in this initial ILD trial will inform further development of therapeutics leveraging the Resokine pathway in RPICs.

An Emerging Pipeline of Product Opportunities

Our Preclinical Immuno-Modulatory Domain Program from the Resokine Pathway: iMod.Fc

We have conducted a series of experiments to understand how various product form modifications enhance exposure and activity of the iMod domain of Resokine. Fc fusion proteins have been successfully commercialized previously by others to enhance exposure while enabling biological activity. We explored this approach by fusing the immunoglobin Fc with one iMod domain, which can form a dimer.

Our Fc fusion experiments have begun to delineate how to enhance the exposure of the iMod domain of Resokine while maintaining activity and provide insights into this domain harboring immuno-modulatory activity. Initial experiments have indicated that Fc fusion proteins can increase exposure and maintain iMod domain activity. We have generated encouraging results for one iMod.Fc in a mouse model of lung inflammation and fibrosis.

Our Discovery Engine for Therapeutic Applications of Physiocrines: Lung and Liver Focused

Our discovery efforts are based on our scientific investigation of Physiocrine pathways. Through a combination of deep sequencing and bioinformatics panning, augmented by proteomic analysis, we identified over 300 naturally occurring Physiocrines. We expressed and purified over 200 of these Physiocrines and evaluated these purified Physiocrines in numerous cell-based assays to determine their activity in important human physiological pathways. In July 2014, a publication in *Science* described a portion of the results from our research, along with our collaborators at Scripps La Jolla, Scripps Florida, Stanford University and the Hong Kong University of Science and Technology.

Our scientists have conducted experiments that demonstrated that the blockade of Physiocrine pathways in rodents resulted in an *in vivo* phenotype characterized by immune cell infiltration or fibrotic disease in the lung or the liver. These data support the concept that Physiocrines may have the potential to inhibit, limit, or otherwise regulate immune cell activity in both the lung and the liver, as well as the subsequent development of fibrosis in these tissues. Accordingly, we are continuing to investigate certain Physiocrines for potential therapeutic applications in both lung and liver indications.

Our Strategy

We aim to capitalize on Physiocrine biology, a new and important area of human health, to develop first-in-class medicines to treat patients with severe diseases characterized by an immune component. Key elements of our strategy include the following:

- ***Leverage our leadership position in Physiocrine biology to develop and commercialize novel, first-in-class medicines for patients affected by severe, rare diseases with significant unmet need.*** We believe our initial focus on severe, rare diseases will allow us to more effectively deploy investor capital for the independent development and commercialization of medicines for the benefit of patients and our stakeholders.
- ***Rapidly and prudently pursue the development and commercialization of Resolaris to treat patients across multiple severe, rare disease indications.*** We are currently evaluating Resolaris in a Phase 1b/2 clinical trial in adult patients with FSHD and expect to report initial results from this clinical trial in the fourth quarter of 2015 or early 2016. In addition, we plan to initiate clinical trials of Resolaris in early onset FSHD and other RMIC indications, including LGMD, as well as other rare diseases with an immune component, such as RPIC indications.
- ***Leverage our discovery engine to build a pipeline of first-in-class Physiocrine medicines to address severe conditions characterized by immune pathway dysfunction or fibrosis.*** We plan to leverage our discovery engine to identify other Physiocrine pathways of interest and select additional potential product candidates for preclinical and clinical investigation in a variety of disease settings on a tissue-by-tissue basis, which may include severe, currently inadequately treated diseases of the lung and liver.

- ***Retain exclusive worldwide commercial rights to our product candidates to pursue autonomous commercialization***. We intend to build a pipeline of product candidates that we can commercialize independently through a relatively small, dedicated commercial organization focused on patient needs and directed at a limited number of physicians who specialize in the treatment of our target patient populations.
- ***Expand our knowledge and intellectual property position in Physiocrine biology by emphasizing continuous scientific and business improvements.*** We intend to aggressively pursue new scientific and therapeutic insights into the potential therapeutic applications of Physiocrines, and to broaden our patent portfolio across this class of novel protein therapeutics and their antibody antagonists.
- ***Build a world class organization oriented to patients and focused on rigorous scientific, clinical and industrial advancements***. We have assembled a world class team with industry-recognized expertise in biology, medicine and the commercialization of innovative and important therapeutics. We intend to continue to build on our leadership position in Physiocrine and immunology-based therapeutics and grow an organization and culture dedicated to the development and commercialization of medicines with the potential to positively transform the lives of patients with severe, rare diseases.

Risks Associated with Our Business

Our ability to implement our business strategy is subject to numerous risks, as more fully described in the section entitled "Risk Factors" immediately following this prospectus summary. These risks include, among others:

- Resolaris, and any other product candidates that we may develop, represent novel therapeutic approaches, which may cause significant delays or may not result in any commercially viable drugs.
- We are highly dependent on the success of Resolaris, which is still in early clinical development. If we are unable to successfully complete or otherwise advance clinical development, obtain regulatory or marketing approval for, or successfully manufacture or commercialize, Resolaris, or experience significant delays in doing so, our business will be materially harmed.
- Data generated in our preclinical studies and patient sample data relating to the Resokine pathway may not be predictive or useful for determining the immuno-modulatory activity or therapeutic effects, if any, of Resolaris in patients, and success in early-stage clinical trials may not be predictive of success in later-stage clinical trials.
- We have incurred significant losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future. We have never generated any revenue from product sales and may never be profitable.
- We will need substantial additional funding. If we are unable to raise capital when needed, we would be forced to delay, reduce or eliminate product development programs or commercialization efforts.
- We have not studied Resolaris or any of our other product candidates in any human clinical trials designed to show efficacy to date.
- We are developing novel product candidates for the treatment of diseases in which there is little clinical drug development experience and, in some cases, are using new endpoints or methodologies. The regulatory pathways for approval are not well defined, and as a result there is greater risk that the outcome of our clinical trials will not be favorable.
- 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.

- If we are unable to obtain and maintain patent, trade secret or other intellectual property protection for our medicines and technology, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize medicines and technology similar or identical to ours, and our ability to successfully commercialize our medicines and technology may be adversely affected.
- If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize, or will be delayed in commercializing, our product candidates, and our ability to generate revenue will be materially impaired.

Implications of Being an Emerging Growth Company

We qualify as an "emerging growth company" as defined in the Jumpstart Our Business Startups Act of 2012, as amended, or the JOBS Act. As an emerging growth company, we may take advantage of specified reduced disclosure and other requirements that are otherwise applicable generally to public companies. These provisions include:

- only two years of audited financial statements in addition to any required unaudited interim financial statements with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure;
- reduced disclosure about our executive compensation arrangements;
- no non-binding advisory votes on executive compensation or golden parachute arrangements; and
- exemption from the auditor attestation requirement in the assessment of our internal control over financial reporting.

We may take advantage of these exemptions for up to five years or such earlier time that we are no longer an emerging growth company. We would cease to be an emerging growth company on the date that is the earliest of (i) the last day of the fiscal year in which we have total annual gross revenues of $1 billion or more; (ii) the last day of our fiscal year following the fifth anniversary of the date of the completion of this offering; (iii) the date on which we have issued more than $1 billion in nonconvertible debt during the previous three years; or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the Securities and Exchange Commission, or SEC. We may choose to take advantage of some but not all of these exemptions. We have taken advantage of reduced reporting requirements in this prospectus. Accordingly, the information contained herein may be different from the information you receive from other public companies in which you hold stock. We have irrevocably elected to "opt out" of the exemption for the delayed adoption of certain 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.

Company and Other Information

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

THE OFFERING

Common stock offered by us	5,360,000 shares.
Common stock to be outstanding immediately after this offering	22,549,739 shares (23,353,739 shares if the underwriters exercise their over-allotment option in full).
Underwriters' option to purchase additional shares	We have granted a 30-day option to the underwriters to purchase up to an aggregate of 804,000 additional shares of common stock to cover over-allotments.
Use of proceeds	We intend to use the net proceeds from this offering to fund our clinical development of Resolaris, to advance our other research, discovery and development activities, and for working capital and general corporate purposes. For a more complete description of our intended use of the proceeds from this offering, see "Use of Proceeds."
Risk factors	You should carefully read "Risk Factors" in this prospectus for a discussion of factors that you should consider before deciding to invest in our common stock.
NASDAQ Global Select Market symbol	"LIFE"

Certain of our existing stockholders, including a stockholder affiliated with one of our directors, have indicated an interest in purchasing and have agreed to purchase an aggregate of 1,070,000 shares of our common stock in this offering at the initial public offering price. The underwriting discount for the shares sold to these investors in the offering will be the same as the underwriting discount for the shares sold to the public.

The number of shares of our common stock to be outstanding after this offering is based on 17,189,739 shares of our common stock outstanding as of December 31, 2014, which includes the conversion of all outstanding shares of redeemable convertible preferred stock, including the shares of our Series E redeemable convertible preferred stock issued in March 2015, into an aggregate of 16,279,859 shares of common stock immediately prior to the completion of this offering and excludes:

- 1,514,471 shares of common stock issuable upon the exercise of stock options outstanding as of December 31, 2014 at a weighted average exercise price of $4.60 per share;
- 25,970 shares of common stock issuable upon the exercise of warrants outstanding as of December 31, 2014 at a weighted average exercise price of $14.44 per share of common stock, which warrants prior to the completion of this offering are exercisable to purchase redeemable convertible preferred stock;
- the issuance of 119,840 shares of common stock to The Scripps Research Institute on March 31, 2015;
- 639,619 shares of common stock issuable upon the exercise of stock options granted to employees, directors and consultants subsequent to December 31, 2014 at a weighted average exercise price of $9.15 per share;

- 94,455 shares of common stock issuable upon the conversion of 751,314 shares of Series D redeemable convertible preferred stock that may be issued under a convertible promissory note issued to an affiliate of our landlord, if the noteholder elects to convert the note in accordance with its terms;
- 1,574,566 shares of common stock reserved for future issuance under our 2015 Stock Option and Incentive Plan, or the 2015 Plan, options to purchase 377,158 shares of which will be issued in connection with this offering at an exercise price equal to the initial public offering price, and which 2015 Plan became effective upon the effectiveness of the registration statement of which this prospectus is a part; and
- 227,623 shares of common stock reserved for future issuance under our 2015 Employee Stock Purchase Plan, or the 2015 ESPP, which became effective upon the effectiveness of the registration statement of which this prospectus is a part.

Unless otherwise indicated, all information in this prospectus reflects or assumes the following:

- the filing of our amended and restated certificate of incorporation and the adoption of our amended and restated bylaws, which will occur immediately prior to the completion of this offering;
- the issuance and sale of 68,166,894 shares of our Series E redeemable convertible preferred stock in March 2015 for aggregate gross proceeds of approximately $76.3 million;
- the conversion of all of our outstanding shares of redeemable convertible preferred stock, including the shares of our Series E redeemable convertible preferred stock issued in March 2015, into 16,279,859 shares of common stock upon the completion of this offering;
- our repayment in cash, upon the completion of this offering, of approximately $2.5 million in principal and accrued interest as of December 31, 2014 under a convertible promissory note issued to an affiliate of our landlord, assuming the note holder does not elect, on or prior to the date of completion of this offering, to forgive all accrued interest under the note and convert the $2.0 million in principal under the note into 751,314 shares of our Series D redeemable convertible preferred stock, which would convert into 94,455 shares of common stock upon the completion of this offering;
- a one-for-7.95413 reverse split of our common stock effected on May 5, 2015; and
- no exercise by the underwriters of their option to purchase up to an additional 804,000 shares of common stock in this offering.

SUMMARY CONSOLIDATED FINANCIAL DATA

The following summary consolidated financial information should be read together with the information under the caption "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our consolidated financial statements and accompanying notes appearing elsewhere in this prospectus. The summary consolidated statement of operations data for the years ended December 31, 2013 and 2014 and the summary consolidated balance sheet data as of December 31, 2014 are derived from our audited consolidated financial statements appearing elsewhere in this prospectus. Our historical results are not necessarily indicative of results that may be expected in the future.

	Years Ended December 31,	
	2013	2014
	(in thousands, except share and per share data)	
Statements of Operations Data:		
Operating expenses:		
Research and development	$ 13,832	$ 16,777
General and administrative	5,710	6,777
Total operating expenses	19,542	23,554
Loss from operations	(19,542)	(23,554)
Other income (expense)	(472)	(796)
Net loss	(20,014)	(24,350)
Accretion to redemption value of redeemable convertible preferred stock	(1,637)	(416)
Net loss attributable to common stockholders	$ (21,651)	$ (24,766)
Net loss per share attributable to common stockholders, basic and diluted (1)	$ (28.39)	$ (29.69)
Weighted average shares outstanding, basic and diluted (1)	762,761	834,221
Pro forma net loss per share attributable to common stockholders, basic and diluted (unaudited) (1)		$ (2.42)
Pro forma weighted average shares outstanding, basic and diluted (unaudited) (1)		10,073,089

(1) See Note 2 to our audited consolidated financial statements included elsewhere in this prospectus for an explanation of the method used to calculate the historical and pro forma net loss per share, basic and diluted, and the number of shares used in the computation of the per share amounts.

	As of December 31, 2014		
	Actual	Pro Forma (1)	Pro Forma As Adjusted (2)
	(in thousands)		
Consolidated Balance Sheet Data:			
Cash, cash equivalents and investment securities	$ 15,853	$ 89,647	$ 157,033
Total assets	20,644	94,438	159,876
Preferred stock warrant liabilities	319	—	—
Convertible promissory note	2,000	—	—
Working capital	6,396	82,994	151,329
Commercial bank debt, net of current portion	5,142	5,142	5,142
Redeemable convertible preferred stock	95,619	—	—
Accumulated deficit	(110,151)	(110,151)	(110,151)
Total stockholders' equity (deficit)	(91,010)	81,207	147,594

(1) Pro forma amounts reflect (i) the filing and effectiveness of our amended and restated certificate of incorporation, (ii) the issuance and sale of 68,166,894 shares of our Series E redeemable convertible preferred stock in March 2015 for aggregate gross proceeds of approximately $76.3 million, (iii) the conversion of all our outstanding shares of redeemable convertible preferred stock, including the shares of our Series E redeemable convertible preferred stock issued in March 2015, into an aggregate of 16,279,859 shares of our common stock immediately prior to the completion of this offering, and the resultant reclassification of our redeemable convertible preferred stock to stockholders' deficit, (iv) the adjustment of our outstanding warrants to purchase redeemable convertible preferred stock into warrants to purchase 25,970 shares of our common stock, and the resultant reclassification of our preferred stock warrant liabilities to additional paid-in capital, a component of total stockholders' equity (deficit) and (v) our repayment in cash, upon the completion of this offering, of approximately $2.5 million in principal and accrued interest as of December 31, 2014 under a convertible promissory note issued to an affiliate of our landlord, assuming the note holder does not elect, on or prior to the date of completion of this offering, to forgive all accrued interest under the note and convert the $2.0 million in principal under the note into 751,314 shares of our Series D redeemable convertible preferred stock, which would convert into 94,455 shares of common stock upon the completion of this offering.

(2) Pro forma as adjusted amounts reflect the pro forma conversion adjustments described in footnote (1) above, as well as the sale of shares of our common stock in this offering at the initial public offering price of $14.00 per share, and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below along with all of the other information contained in this prospectus, 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 purchase our common stock. If any of the adverse events described in the following risk factors actually occurs, our business, results of operations and financial condition may suffer significantly. As a result, the trading price of our common stock could decline, and you may lose all or part of your investment in our common stock. Additional risks or uncertainties not presently known to us or that we do not currently deem material may also impair our business operations.

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

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

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

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

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

- establishing sales and marketing capabilities after obtaining any regulatory approval to gain market acceptance; and
- developing therapeutics for rare and more common diseases or indications beyond those addressed by our current product candidates.

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

We are highly dependent on the success of Resolaris, our first clinical product candidate, which is still in early clinical development. If we are unable to successfully complete or otherwise advance clinical development, obtain regulatory or marketing approval for, or successfully commercialize, Resolaris, or experience significant delays in doing so, our business will be materially harmed.

To date, we have expended significant time, resources and effort on the discovery and development of Resolaris, including conducting preclinical studies and our Phase 1 clinical trial, and initiating and preparing for additional clinical trials. We have not yet commenced or completed any evaluation of Resolaris in human clinical trials designed to demonstrate efficacy to the satisfaction of the FDA. We currently generate no revenue from the sale of any product, and our ability to generate product revenues and to achieve commercial success, which we do not expect will occur for many years, if ever, will initially depend on our ability to successfully develop, obtain regulatory approval for and commercialize Resolaris for the treatment of one or more of our target rare disease indications in the United States and any foreign jurisdictions. Before we can market or sell Resolaris in the United States or foreign jurisdictions, we will need to commence and complete additional clinical trials (including larger, pivotal trials, which we have not yet commenced), manage clinical and manufacturing activities, obtain necessary regulatory approvals from the FDA in the United States and from similar regulatory authorities in other jurisdictions, obtain adequate clinical and commercial manufacturing supplies, build commercial capabilities, which may include entering into a marketing collaboration with a third party, and in some jurisdictions, obtain reimbursement authorization, among other things. We cannot assure you that we will be able to successfully complete the necessary clinical trials, obtain regulatory approvals, secure an adequate commercial supply for, or otherwise successfully commercialize, Resolaris. If we do not receive regulatory approvals for Resolaris, and even if we do obtain regulatory approvals, we may never generate significant revenues, if any, from commercial sales. If we fail to successfully commercialize Resolaris, we may be unable to generate sufficient revenues to sustain and grow our company, and our business, prospects, financial condition and results of operations will be adversely affected.

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

Our scientists discovered the Resokine pathway using *in vivo* screening systems designed to test potential immuno-modulatory activity in animal models of severe immune activity or inflammation, combined with data relating to the potential blockade of the Resokine pathway in a population of patients with myopathy that occurs in a particular rare disease, anti-synthetase syndrome, with Jo-1 antibodies. Translational medicine, or the application of basic scientific findings to develop therapeutics that promote human health, is subject to a number of inherent risks. In particular, scientific hypotheses formed from non-clinical 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 studied the activity of the Resokine pathway in patients with rare genetic myopathies with an immune component, which forms the basis for our first clinical trial of Resolaris in facioscapulohumeral dystrophy, or FSHD, nor have we evaluated the activity of the Resokine pathway in patients with interstitial lung disease, or ILD. Our knowledge of the activity of this pathway in Jo-1 antibody patients may not be applicable to our target patient populations in rare myopathies with an immune component, or RMICs, or rare pulmonary diseases with an immune component, or RPICs. In addition, our classification of diseases based on the existence of immune cell invasion (RMICs and RPICs) and our hypothesis that these represent potential indications for Resolaris 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 immono-modulatory domain, or iMod domain, may not be substantiated in other animal models or in clinical trials. Any failure to demonstrate in controlled clinical trials the requisite safety and efficacy of Resolaris or other product candidates that we may develop will adversely affect our business, prospects, financial condition and results of operations.

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

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

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

Our initial clinical focus is on the development of Physiocrine-based therapeutics for the treatment of rare diseases, including FSHD, where patients may benefit from the activation of immuno-modulatory pathways. There are currently no approved treatments for FSHD or other rare disease indications that we intend to initially pursue, such as limb-girdle muscular dystrophy, or LGMD. As a result, the design and conduct of clinical trials for these indications are subject to increased risk, and we may experience setbacks with our ongoing or planned clinical trials for Resolaris or other product candidates that we may develop because of the limited clinical experience in our target indications. In particular, regulatory authorities in the United States and European Union have not issued definitive guidance as to how to measure and achieve efficacy. In addition, the protocol for our Phase 1b/2 clinical trial of Resolaris in adult patients with FSHD includes the use of magnetic resonance imaging, or MRI, data as a measure of potential immuno-modulatory effects of Resolaris in diseased muscle tissue. Regulators have not yet determined that such data in FSHD patients signifies a clinical meaningful result or can support regulatory approvals. We may not achieve the pre-specified endpoint with statistical significance in our planned clinical trials of Resolaris in this indication or in other indications where there is limited or no regulatory guidance regarding appropriate clinical endpoints, which would decrease the chance of obtaining marketing approval for Resolaris. Additionally, it is difficult to establish clinically relevant endpoints for some of these indications because it may take a long time before any therapeutic effects of a drug can be observed.

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

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

Before obtaining marketing approval from regulatory authorities for the sale of our product candidates, we must conduct extensive clinical trials to demonstrate the safety and efficacy of the product candidates in humans. Clinical trials are expensive, time-consuming, often delayed and uncertain as to outcome. We cannot guarantee that our ongoing and planned clinical trials of Resolaris in RMICs or RPICs, or any other clinical trials that we may plan to conduct, will be initiated or conducted as planned or completed on schedule, if at all. Following our submission of an investigational new drug application, or IND, to the Division of Neurology Products at the FDA to evaluate Resolaris in a Phase 1b/2 trial in adult patients with FSHD in the United States, our IND was placed on full clinical hold to address the non-clinical issue of the comparability of the drug substance used in our preclinical toxicology studies to that used in our Phase 1 clinical trial and proposed for use in the U.S. clinical trial in FSHD patients. We responded to the FDA's comparability request, and, in January 2015, our IND was removed from full clinical hold, allowing us to initiate the Phase 1b/2 trial in the United States. Our IND remains on partial clinical hold, which prohibits the evaluation of Resolaris at doses higher than our proposed 3.0 mg/kg dose pending our submission of additional non-clinical data to the FDA and the FDA's review of that data. We intend to submit a complete response to address this concern in the second half of 2015. We cannot assure you that the FDA will deem our response to be a complete response or that it will determine to lift the partial clinical hold. Although we do not expect the partial clinical hold to have a material impact on our current clinical development timeline for Resolaris in FSHD because we do not intend to evaluate Resolaris at doses higher than 3.0 mg/kg in the current clinical trial in the United States, any inability to initiate or complete our clinical trial of Resolaris in adult patients with FSHD in the United States, as a result of the partial clinical hold 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 Resolaris.

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

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

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

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

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

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

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

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

A key element of our strategy is to leverage our discovery engine to identify tRNA synthetases that exhibit activity in physiological disease pathways of interest, and to develop purified forms of these proteins that are suitable for therapeutic application. A significant portion of the research that we are conducting involves new compounds and drug discovery methods, including our proprietary technology. Our drug discovery activities using our proprietary technology may not be successful in identifying proteins that are useful in treating rare or more common 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 medicines that will receive marketing approval and achieve market acceptance.

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

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

Identifying and qualifying patients to participate in our ongoing and planned clinical trials of Resolaris and any other clinical trials that we may conduct for our product candidates is critical to our success. In particular, each of the conditions for which we currently plan to evaluate Resolaris is a rare disease with limited patient pools from which to draw for clinical trials. For example, while estimates of FSHD prevalence vary, studies exploring the topic have identified average prevalence rates of approximately one in 17,000. Applying this rate to the U.S. population, as of November 1, 2014, yields a domestic FSHD population of approximately 19,000. The eligibility criteria for our clinical trials, such as the requirement of at least one skeletal muscle in the lower extremities displaying an inflammatory immune response by MRI for enrollment in our ongoing Phase 1b/2 clinical trial of Resolaris in adult patients with FSHD, may further limit the pool of available participants in the trial. 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.

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

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

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

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

Additionally, if patients are unwilling to participate in our clinical trials because of negative publicity from adverse events in 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 a sufficient number of patients to conduct our clinical trials as planned for any reason, we may need to delay, limit or terminate ongoing or planned clinical trials, any of which would have an adverse effect on our business, prospects, financial condition and results of operations.

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

Undesirable side effects caused by Resolaris and any other product candidates that we may discover or develop, or safety or toxicity issues that we may experience 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. For example, in its partial clinical hold letter, the FDA has requested that, to support clinical trials of Resolaris at doses higher than our proposed 3.0 mg/kg dose, we will need to provide additional non-clinical data demonstrating that certain rodent deaths in our GLP safety studies of Resolaris at the highest doses administered to rodents were not drug-related or to propose a human clinical monitoring strategy acceptable to the FDA to prevent serious toxicity in humans. We intend to submit a complete response to address this concern regarding rodent deaths in the second half of 2015. Any failure to proceed with clinical testing of Resolaris at the doses required to demonstrate efficacy will impair our ability to obtain regulatory approval.

In our Phase 1 clinical trial, we observed low levels of antibodies to Resolaris in some subjects in response to the administration of Resolaris. The development of higher levels of such antibodies over a longer course of treatment may ultimately limit the efficacy of Resolaris and trigger a negative autoimmune response, including the development of anti-synthetase syndrome. Anti-synthetase syndrome can include one or more of the following clinical features: ILD, inflammatory myopathy and inflammatory polyarthritis. Other symptoms which may occur in this setting include fever, weight loss, fatigue, Raynaud's phenomenon of the digits, rash and difficulty swallowing. Additionally, our product candidates are designed to be administered by intravenous injection, which may cause side effects, including acute immune responses and injection site reactions. The risk of adverse immune responses remains a significant concern for protein therapeutics, and we cannot assure that these or other risks will not occur in any of our clinical trials for Resolaris or other product candidates we may develop. There is also a risk of delayed adverse events as a result of long-term exposure to protein therapeutics that must be administered repeatedly for the management of chronic conditions, such as the development of antibodies, which may occur over time. If any such

adverse events occur, which may include the development of anti-synthetase syndrome from antibodies, further advancement of our clinical trials could be halted or delayed, which would have a material adverse effect on our business, prospects, financial condition and results of operations.

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

- regulatory authorities may withdraw approvals of such products;
- regulatory authorities may require additional warnings on the label;
- we may be required to create a REMS plan, which could include a medication guide outlining the risks of such side effects for distribution to patients, a communication plan for healthcare providers, or other elements to assure safe use;
- we could be sued and held liable for harm caused to patients; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the particular product candidate, if approved, and could significantly harm our business, prospects, financial condition and results of operations.

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

All entities involved in the preparation of therapeutics for clinical trials or commercial sale, including our existing contract manufacturers 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. For example, a manufacturing campaign of our product candidate by one of our contract manufacturers did not meet specifications set for drug substance. Our contract manufacturer is in the process of starting a separate, additional manufacturing campaign as a replacement for additional drug substance not available from the earlier campaign. While no material that did not meet specifications was administered to a subject, such events could lead to delays in our clinical trials for Resolaris. We or our contract manufacturers must supply all necessary documentation in support of a biologics license application, or BLA, on a timely basis and must adhere to the FDA's good laboratory practices, or GLP, and cGMP regulations enforced by the FDA through its facilities inspection program. Some of our contract manufacturers have not produced a commercially-approved product and therefore have not undergone the requisite FDA or other regulatory pre-approval inspection to do so. The facilities and quality systems of our contract manufacturers and other third-party contractors must pass a pre-approval inspection for compliance with applicable regulations as a condition of regulatory approval of our product candidates. In addition, the regulatory authorities may, at any time, audit or inspect a manufacturing facility involved with the preparation of our product candidates or the associated quality systems for compliance with the regulations applicable to the activities being conducted. If these facilities do not pass a pre-approval plant inspection, FDA approval of the products will not be granted.

The regulatory authorities also may, at any time following approval of a product for sale, audit the facilities in which the product is manufactured. If any such inspection or audit of our facilities or those of our third-party contractors 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 third-party manufacturers fail to maintain regulatory compliance, the FDA can impose regulatory sanctions including, among other things, refusal to approve a pending application for a new drug product or 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 Resolaris and any other Physiocrine-based therapeutics that we may develop presents challenges associated with biologics production, including the inherent instability of larger, more complex molecules and the need to ensure uniformity of the drug substance produced in different facilities or across different batches. We are also currently in the process of changing cell lines for the production of Resolaris in connection with our potential engagement of a new contract manufacturer to meet our projected needs for pivotal clinical trials and a commercial chemistry, manufacturing and controls specification, which may present production challenges or delays. Furthermore, although Physiocrines represent a class of proteins that may share immuno-modulatory properties in various physiological pathways, each Physiocrine has a different structure and may have unique manufacturing requirements that are not applicable across the entire class. For example, Fc fusion proteins, such as iMod.Fc, include an additional antibody domain to improve pharmacokinetic, or PK, characteristics, and may therefore require a more complex and time-consuming manufacturing process than other Physiocrines. As a result, 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 manufacturing stoppage or delay, or any inability to consistently manufacture adequate supplies of our product candidates for our ongoing or planned clinical trials or on a commercial scale will harm our business, prospects, financial condition and results of operations.

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

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

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

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

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

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

We may not elect or be able to take advantage of any expedited development or regulatory review and approval processes available to product candidates granted breakthrough therapy or fast track designation by the FDA.

We are evaluating the possibility of seeking breakthrough therapy or fast track designation for Resolaris and any other product candidates that we may develop, although we may elect not to do so. A breakthrough therapy program is for a product candidate intended to treat a serious or life-threatening condition, and preliminary clinical evidence indicates that the product candidate may demonstrate substantial improvement on a clinically significant endpoint(s) over available therapies. A fast track program is for a product candidate that treats a serious or life-threatening condition, and nonclinical or clinical data demonstrate the potential to address an unmet medical need. Although we believe Resolaris and other product candidates that we may develop from our discovery engine may qualify under either or both of the breakthrough therapy and fast track programs, we may elect not to pursue either of these programs, and even if we do, 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 do 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 Resolaris or any other product candidates that we discover and develop are approved, they will be subject to ongoing regulatory requirements for manufacturing, labeling, packaging, storage, advertising, promotion, sampling, record-keeping, conduct of post-marketing studies, and submission of safety, efficacy, and other post-market information, including both federal and state requirements in the United States and requirements of comparable foreign regulatory authorities.

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

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

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

The holder of an approved BLA, NDA or MAA must submit new or supplemental applications and obtain approval for certain changes to the approved product, product labeling, or manufacturing process. We could also be asked to conduct post-marketing clinical trials to verify the safety and efficacy of our products in general or in specific patient subsets. If original marketing approval were obtained through an accelerated approval pathway,

we could be required to conduct a successful post-marketing clinical trial to confirm clinical benefit for our products. An unsuccessful post-marketing study or failure to complete such a trial could result in the withdrawal of marketing approval.

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

- issue untitled or warning letters;
- impose civil or criminal penalties;
- suspend or withdraw regulatory approval;
- suspend any of our ongoing clinical trials;
- refuse to approve pending applications or supplements to approved applications submitted by us;
- impose restrictions on our operations, including closing our contract manufacturers' facilities; or
- seize or detain products, or require a product recall.

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

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

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

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

Physicians may independently file individual patient INDs for Resolaris or one of our other product candidates. We may disagree with a physician's or the FDA's conclusion that our product candidate is suitable

for evaluation under a particular individual patient IND, and any decision by us not to make our product candidate available for evaluation under this setting may subject us to negative publicity or market perception.

Risks related to our financial condition and capital requirements

We have incurred significant losses since our inception and anticipate that we will continue to incur significant losses for the foreseeable future.

We are a clinical stage biotherapeutics company, and we have not yet generated any revenues from product sales. We have incurred net losses in each year since our inception in 2005, including net losses of $20.0 million and $24.4 million for the years ended December 31, 2013 and 2014, respectively. As of December 31, 2014, we had an accumulated deficit of $110.2 million.

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

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

- continue our research and preclinical and clinical development of Resolaris, our lead product candidate, or any other product candidates that we may develop;
- continue our current clinical trial of Resolaris in adult patients with FSHD and initiate and conduct our planned additional clinical trials of Resolaris in FSHD, LGMD and other RMICs;
- initiate and conduct any additional preclinical studies, clinical trials or other studies for Resolaris and any other product candidates that we may develop;
- further develop the manufacturing process for our product candidates;
- change or add additional manufacturers, including manufacturers of quantities of drug substance suitable for pivotal clinical trials and commercialization;
- seek regulatory and marketing approvals for our product candidates that successfully complete clinical trials;
- establish a sales, marketing and distribution infrastructure to commercialize any products for which we may obtain marketing approval;
- seek to identify and validate additional product candidates;
- make milestone or other payments under our in-license agreements;
- maintain, protect and expand our portfolio of owned and in-licensed intellectual property;
- acquire or in-license other product candidates and technologies;
- attract and retain skilled personnel;

- create additional infrastructure to support our operations as a public company and our product development and planned future commercialization efforts; and
- experience any delays or encounter challenges with any of the above.

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

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

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

- completing research, preclinical development and clinical development of Resolaris and other product candidates;
- seeking and obtaining regulatory and marketing approvals for product candidates for which we complete clinical trials;
- developing a sustainable, scalable, reproducible, and transferable manufacturing process for Resolaris and any other product candidates that we may develop;
- establishing and maintaining supply and manufacturing relationships with third parties that can provide products and services that are adequate in both amount and quality to support clinical development and the market demand for our product candidates, if approved;
- launching and commercializing product candidates for which we obtain regulatory and marketing approval, by establishing a sales force, marketing and distribution infrastructure;
- maintaining, protecting and expanding our portfolio of intellectual property rights, including patents, trademarks, trade secrets and know-how;
- obtaining market acceptance of Physiocrine therapeutics and our product candidates as viable treatment options for our target indications;
- addressing any competing technological and market developments;
- implementing additional internal systems and infrastructure, as needed;
- identifying and validating new Physiocrine therapeutic product candidates;
- attracting, hiring and retaining qualified personnel; and
- negotiating favorable terms in any licensing, collaboration or other arrangements into which we may enter.

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

expect, or the reasonably accepted population for treatment is narrowed by competition, physician choice or treatment guidelines, we may not generate significant revenue from sales of such products, even if approved. Even if we are able to generate revenues from the sale of any approved products, we may not become profitable and may need to obtain additional funding to continue operations.

Even if this offering is successful, we will need to raise additional funding, which may not be available on acceptable terms, or at all. Failure to obtain this necessary capital when needed may force us to delay, limit or terminate our product development efforts or other operations.

We are currently advancing Resolaris through clinical development and conducting preclinical development activities directed at the identification and selection of additional Physiocrine-based therapeutic candidates. The development of protein therapeutics is expensive, and we expect our research and development expenses to increase substantially in connection with our ongoing activities, particularly as we advance Resolaris into further clinical trials in multiple indications.

As of December 31, 2014, our cash, cash equivalents and investments were approximately $15.9 million. We estimate that the net proceeds from this offering will be approximately $66.4 million, based on the initial public offering price of $14.00 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us. We expect that the net proceeds from this offering and our existing cash, cash equivalents and investments will be sufficient to fund our current operations through at least the next 12 months. However, our operating plan may change as a result of many factors currently unknown to us, and we may need to seek additional funds sooner than planned, through public or private equity or debt financings, government or other third-party funding, marketing and distribution arrangements and other collaborations, strategic alliances and licensing arrangements or a combination of these approaches. Our future funding requirements will depend on many factors, including but not limited to:

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

In any event, we will require additional capital to complete additional clinical trials, including larger, pivotal clinical trials, to obtain regulatory approval for, and to commercialize, our product candidates. 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 or otherwise capitalize on our business opportunities, as desired, which could materially affect our business, financial condition and results of operations.

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

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

We are party to a loan and security agreement that contains operating covenants that may restrict our business and financing activities.

In April 2012, we entered into a loan and security agreement with Silicon Valley Bank, which was subsequently amended in July 2013, pursuant to which we have been extended term loans in the aggregate principal amount of $10.0 million. Borrowings under this loan and security agreement are secured by substantially all of our assets, excluding certain intellectual property rights. The loan and security agreement restricts our ability, among other things, to:

- sell, transfer or otherwise dispose of any of our business or property, subject to limited exceptions;
- make material changes to our business or management;
- enter into transactions resulting in significant changes to the voting control of our stock;
- make certain changes to our organizational structure;
- consolidate or merge with other entities or acquire other entities;
- move our principal office location or add new office locations;
- incur additional indebtedness or create encumbrances on our assets, subject to limited exceptions;
- pay dividends, other than dividends paid solely in shares of our common stock, or make distributions on and, in certain cases, repurchase our stock;
- enter into transactions with our affiliates, subject to limited exceptions;
- repay subordinated indebtedness; or
- make certain investments.

In addition, we are required under our loan agreement to comply with various affirmative operating covenants. The operating covenants and restrictions and obligations in our loan and security 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 these covenants could result in a default under the loan and security agreement, which could cause all of the outstanding indebtedness under the facility to become immediately due and payable.

If we are unable to generate sufficient cash available to repay our debt obligations when they become due and payable, either as or when such obligations become due, when they mature, or in the event of a default, we may not be able to obtain additional debt or equity financing on favorable terms, if at all, which may negatively impact our business operations and financial condition.

Risks related to our reliance on third parties

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

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

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 on a third party to manufacture our clinical supply of Resolaris, and we intend to rely on third parties to produce non-clinical, clinical and commercial supplies of any future product candidate.

We do not have, nor do we plan to acquire, the infrastructure or capability internally to manufacture our nonclinical and clinical quantities of our product candidates, and we lack the resources and the capability to manufacture any of our product candidates on a clinical or commercial scale. Reliance on third-party manufacturers 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 manufacturers 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 third-party manufacturers or suppliers caused by conditions unrelated to our business or operations, including the insolvency or bankruptcy of the manufacturer 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 manufacturer may require licenses to manufacture our product candidates or components thereof if the applicable manufacturing processes are not owned by the manufacturer 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 rely on a single manufacturer for Resolaris in our clinical trials and are currently in discussions with an additional contract manufacturer to meet our projected needs for anticipated pivotal clinical trials and larger scale commercial manufacturing. We do not have long-term contracts with our manufacturers, and our manufacturers may terminate their agreements with us for a variety of reasons. Furthermore, 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 manufacturers fail to meet contractual requirements, and we are unable to secure one or more replacement manufacturers 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 third-party manufacturers 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 manufacturers, transfer manufacturing procedures to these alternative manufacturers, and demonstrate comparability of material produced by such new manufacturers. New manufacturers of any product would be required to qualify under applicable regulatory requirements. These manufacturers 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 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 CROs are required to comply with GCPs for conducting, recording and reporting the results of IND-enabling studies and 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 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 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 CROs are not our employees, and we are therefore unable to directly monitor whether or not they devote sufficient time and resources to our clinical and nonclinical programs. These CROs 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 CROs do not successfully carry out their contractual duties or obligations, fail to meet expected deadlines, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements, or for any other reasons, our clinical trials may be extended, delayed or terminated, and we may not be able to obtain regulatory approval for, or successfully commercialize our product candidates. As a result, our financial results would be harmed, our costs could increase, our ability to generate revenues could be delayed and the commercial prospects for our product candidates will be adversely affected.

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

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

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

Risks related to the commercialization of our product candidates

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

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

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

- our inability to recruit and retain adequate numbers of effective sales and marketing personnel;
- the inability of sales personnel to obtain access to physicians or persuade adequate numbers of physicians to prescribe any future medicines;

- the lack of complementary medicines to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

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

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

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

No manufacturer currently has the experience or ability to produce our product candidates at commercial levels. We or our contract manufacturers will need to develop a scalable manufacturing process for Resolaris or any other product candidates that we may develop and commercialize. We may run into technical or scientific issues related to manufacturing or development that we may be unable to resolve in a timely manner or with available funds. If we or our manufacturing partners are unable to scale the manufacturing process to produce commercial quantities of our product candidates, or our manufacturing partners do not pass required regulatory pre-approval inspections, our commercialization efforts will be harmed.

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

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

We are engaged in the development of medicines for severe, rare diseases, which is a competitive and rapidly changing field. We have competitors both in the United States and internationally, including major multi-national pharmaceutical companies, biotechnology companies and universities and other research institutions. We expect to compete with various companies, academic institutions and other organizations that have products in development for some of our target RMIC indications. For example, although there are currently no approved products for the treatment of FSHD, Acceleron Pharma Inc. is developing a clinical candidate, ACE-083, a locally acting protein therapeutic designed to increase muscle mass and strength in patients with neuromuscular disorders and other diseases characterized by a loss of muscle function, including FSHD. In addition, Facio

Therapies recently announced its plans to screen chemical libraries to identify chemical compounds that will boost the expression of proteins known to repress one of the causal genes responsible for FSHD. We may also face competition from numerous companies in the field of RPICs, including several companies that currently market Esbriet (pirfenidone) and Nintedanib, both of which were approved by the FDA for the treatment of ILD in October 2014. Many larger companies, universities and private and public research institutions are also actively engaged in the development of therapeutics to address muscle loss and muscle weakness in a variety of indications.

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

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

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

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

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

- the potential efficacy and potential advantages over alternative treatments;

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

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

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

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

Outside the United States, international sales are generally subject to extensive governmental price controls and other market regulations, and we believe the increasing emphasis on cost-containment initiatives in Europe, Canada, and other countries has and will continue to put pressure on the pricing and usage of our product candidates. In many countries, the prices of medical products are subject to varying price control mechanisms as part of national health systems. In general, the prices of medicines under such systems are substantially lower than in the United States. Other countries allow companies to fix their own prices for medicines, but monitor and control company profits. Additional foreign price controls or other changes in pricing regulation could restrict the

amount that we are able to charge for our product candidates. Accordingly, in markets outside the United States, the reimbursement for our products may be reduced compared with the United States and may be insufficient to generate commercially reasonable revenues and profits. Net prices for medicines may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that currently restrict imports of medicines from countries where they may be sold at lower prices than in the United States.

Moreover, increasing efforts by governmental and third-party payors, in the United States and abroad, to cap or reduce healthcare costs may cause such organizations to limit both coverage and level of reimbursement for new products and, as a result, they may not cover or provide adequate payment for our product candidates. We expect to experience pricing pressures in connection with the sale of any of our product candidates, due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative changes. 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.

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

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

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

Risks related to our intellectual property

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

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

We have sought to protect our proprietary position by filing patent applications in the United States and abroad related to our novel technologies and product candidates that are important to our business. This process is expensive and time consuming, and we may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection.

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

If the patent applications we own or have in-licensed that relate to our programs or product candidates do not issue as patents, if their breadth or strength of protection is threatened, or if they fail to provide exclusivity for our product candidates, it could dissuade companies from collaborating with us to develop product candidates, and threaten our ability to commercialize future products. We cannot offer any assurances about which, if any, patents will issue, the breadth of any such patents or whether any issued patents will be found invalid and unenforceable or will be threatened by third parties. Any successful opposition to these patents or any other patents owned by or licensed to us could deprive us of rights necessary for the successful commercialization of any product candidates that we may develop. In addition, patents have a limited term. In the United States, the natural expiration of a patent is generally 20 years after it is filed. Although various extensions may be available, the life of a patent, and the protection it affords, is limited. Even if a patent does issue for any of our pending patent applications, possible delays in regulatory approvals could mean that the period of time during which we could market a product candidate under patent protection could be reduced from what we generally would expect. Since patent applications in the United States and most other countries are

confidential for a period of time after filing, and some remain so until issued, we cannot be certain that we were the first to file any patent application related to a product candidate. Furthermore, if third parties have filed such patent applications, an interference proceeding in the United States can be initiated by a third party to determine who was the first to invent any of the subject matter covered by the patent claims of our applications. Even if patents covering aspects of our product candidates are obtained, once the patent life has expired for a product, we may be open to competition from generic medications.

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

If we are unable to prevent material disclosure of the non-patented intellectual property related to our technologies to third parties, and there is no guarantee that we will have any such enforceable trade secret protection, we may not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, results of operations and financial condition.

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

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

Our commercial success depends in part on our avoiding infringement of the patents and proprietary rights of third parties. There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, oppositions and inter partes reexamination proceedings before the United States Patent and Trademark Office, or USPTO, and corresponding foreign patent offices. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in

which we are pursuing development candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the patent rights of third parties.

Third parties may assert that we are employing their proprietary technology without authorization. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our product candidates. Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that our product candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. If any third-party patents were held by a court of competent jurisdiction to cover the manufacturing process of any of our product candidates, any molecules formed during the manufacturing process or any final product itself, the holders of any such patents may be able to block our ability to commercialize such product candidate unless we obtained a license under the applicable patents, or until such patents expire.

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

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize one or more of our product candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, pay royalties, redesign our infringing products or obtain one or more licenses from third parties, which may not be able to be obtained on reasonable commercial terms or at all, or require substantial time and monetary expenditure.

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

We believe that we have rights to intellectual property, through licenses from third parties and under patents that we own, that is necessary or useful to develop our product candidates. Because our programs may involve additional product candidates that may require the use of proprietary rights held by third parties, the growth of our business will likely depend in part on our ability to acquire, in-license or use these proprietary rights. In addition, our product candidates may require specific formulations to work effectively and efficiently and these rights may be held by others. We may be unable to acquire or in-license any compositions, methods of use, processes or other third-party intellectual property rights from third parties that we identify on reasonable commercial terms or at all. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of more established companies are also pursuing strategies to license or acquire third-party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources and greater clinical development and commercialization capabilities.

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

In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment. If we are unable to successfully obtain rights to required third-party intellectual property rights, our business, financial condition and prospects for growth could suffer.

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

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

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

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

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the license agreement;
- the sublicensing of patent and other rights under our collaborative development relationships;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;

- the ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our licensors and us and our sublicensees or partners, if any; and
- the priority of invention of patented technology.

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

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

Competitors may infringe or otherwise violate our patents, the patents of our licensors or our other intellectual property rights. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. Any claims that we assert against perceived infringers could also provoke these parties to assert counterclaims against us alleging that we infringe their intellectual property rights. In addition, in an infringement proceeding, a court may decide that a patent of ours or our licensors is not valid, is unenforceable or is not infringed, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated or interpreted narrowly and could put our patent applications at risk of not issuing.

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

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock.

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

We employ individuals who were previously employed at universities or other biotechnology or pharmaceutical companies, including our competitors or potential competitors. Although we try to ensure that

our employees, consultants and independent contractors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed intellectual property, including trade secrets or other proprietary information, of any of our employee's former employer or other third parties. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, which could adversely impact our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

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

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

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

On September 16, 2011, the Leahy-Smith America Invents Act, or the Leahy-Smith Act, was signed into law. The Leahy-Smith Act includes a number of significant changes to U.S. patent law, including provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. The USPTO is currently developing regulations and procedures to govern administration of the Leahy-Smith Act, and many of the substantive changes to patent law associated with the Leahy-Smith Act, and in particular, the first to file provisions, were enacted March 16, 2013. Although it is not clear what, if any, impact the Leahy-Smith Act will have on the operation of our business, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business and financial condition.

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

We have filed a U.S. trademark application for the Resolaris mark but it has not yet matured to registration, and we have yet to file any foreign trademark applications for the Resolaris mark. Although, the USPTO has examined our U.S. application for the Resolaris mark and there are no outstanding objections to the application, comparable agencies in foreign jurisdictions may raise objections to our applications. Although we would be given an opportunity to respond to those objections, we may be unable to overcome such objections.

In addition, in the USPTO and in comparable agencies in many foreign jurisdictions, third parties are given an opportunity to oppose pending trademark applications and to seek to cancel registered trademarks. Opposition or cancellation proceedings have been filed and may in the future be filed against certain of our trademarks, and our trademarks may not survive such proceedings. Furthermore, third parties have alleged, and may allege in the future, that Resolaris in particular or any other trademark or trade name that we elect to use for our product candidates, may cause confusion in the marketplace. Specifically, Alexion Pharmaceuticals ("Alexion") recently sent a letter to our counsel alleging that our anticipated use of the Resolaris trademark would cause patients, practitioners and researchers to mistakenly associate us with Alexion or its Soliris product. Alexion claims ownership of a U.S. trademark registration for its Soliris mark. Alexion concluded its letter by requesting that we select a new name for our Resolaris product and withdraw our pending trademark application for the mark. We evaluate such actual and potential allegations in the course of our business, and such evaluations may cause us to change our commercialization or branding strategy for our product candidates, which may require us to incur additional costs. In particular, we are currently assessing Alexion's allegations and will determine whether we need to, or should, select a different name for the product or contest any trademark enforcement actions by Alexion. Moreover, any name we propose to use with our product candidates in the United States must be approved by the FDA, regardless of whether we have registered it, or applied to register it, as a trademark. The FDA typically conducts a review of proposed product names, including an evaluation of potential for confusion with other product names. If the FDA objects to any of our proposed proprietary product names, we may be required to expend significant additional resources in an effort to identify a suitable substitute name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA.

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

Filing, prosecuting and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our products and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Risks related to our business operations

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

We are highly dependent on principal members of our executive team listed under "Management" located elsewhere in this prospectus, the loss of whose services may adversely impact the achievement of our objectives. Additionally, our principal financial and accounting officer is a consultant and we may face conflicts of interest as he allocates his time across various interests. While we have entered into employment agreements with each of our other 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 executives 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, 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, many of our employees have become or will soon become vested in a substantial amount of stock or number of stock options. Our employees may be more likely to leave us if the shares they own or the shares underlying their vested options have significantly appreciated in value relative to the original purchase prices of the shares or the exercise prices of the options, or if the exercise prices of the options that they hold are significantly below the market price of our common stock. Further, our employees' ability to exercise those options and sell their stock in a public market after the closing of this offering may result in a higher than normal turnover rate.

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

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

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

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

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

We have recently increased the size of our management team and as of April 1, 2015, we had 49 full-time employees. As we continue our Phase 1b/2 clinical trial of Resolaris in adult patients with FSHD, prepare for additional clinical trials of Resolaris and expand our other clinical development activities, as well as begin our operations as a public company, we expect to increase our full-time employee base and to hire more consultants and contractors. In addition to certain members of our management team being relatively new to our company, our management may need to divert a disproportionate amount of its attention away from our day-to-day activities and devote a substantial amount of time to managing these growth activities. We may not be able to effectively manage the expansion of our operations, which may result in weaknesses in our infrastructure, operational mistakes, loss of business opportunities, loss of employees and reduced productivity among remaining employees. Our expected growth could require significant capital expenditures and may divert financial resources from other projects, such as the conduct of additional clinical activities for Resolaris and the development of additional product candidates. If our management is unable to effectively manage our growth, our expenses may increase more than expected, our ability to generate or grow revenues could be reduced, and we may not be able to implement our business strategy. Our future financial performance and our ability to develop and commercialize product candidates and compete effectively will depend, in part, on our ability to effectively manage any future growth.

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

Because we have limited resources, we may forego or delay pursuit of certain strategic opportunities or opportunities with certain programs or product candidates or for indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. In addition, we may elect to pursue a research, clinical or commercial strategy that ultimately does not yield the results that we desire. Our spending on current and future research and development programs for product candidates may not result in any commercially viable products. If we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through strategic collaboration, licensing or other royalty arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate, or we may allocate internal resources to a product candidate in a therapeutic area or market in which it would have been more advantageous to enter into a partnering arrangement. Any failure to allocate resources or capitalize on strategies in a successful manner will have an adverse impact on our business.

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

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

this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to comply with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

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

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

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

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

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

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

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties.

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

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

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

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

As a public company, we will incur significant legal, accounting and other expenses that we did not incur as a private company. In addition, the Sarbanes-Oxley Act of 2002, or Sarbanes-Oxley Act, as well as rules subsequently implemented by the Securities and Exchange Commission, or SEC, and The Nasdaq Global Select Market have imposed various requirements on public companies. In July 2010, the Dodd-Frank Wall Street Reform and Consumer Protection Act, or the Dodd-Frank Act, was enacted. There are significant corporate governance and executive compensation related provisions in the Dodd-Frank Act that require the SEC to adopt additional rules and regulations in these areas such as "say on pay" and proxy access. Recent legislation permits smaller "emerging growth companies" to implement many of these requirements over a longer period and up to five years from the pricing of this offering. We intend 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 obtain director and officer liability insurance and we may be required to incur substantial costs to maintain our current levels of such coverage.

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

Our results of operations could be adversely affected by general conditions in the global economy and in the global financial markets. The recent global financial crisis caused extreme volatility and disruptions in the capital and credit markets. A severe or prolonged economic downturn, such as the recent global financial crisis, could result in a variety of risks to our business, including inability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy could also strain our manufacturers, possibly resulting in supply disruption. Any of the foregoing could harm our business and we cannot anticipate all of the ways in which the current economic climate and financial market conditions could adversely impact our business.

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

We are located in San Diego, California, and our clinical supply of Resolaris is currently produced in India. We currently anticipate that if Resolaris receives marketing approval, commercial production may take place in the United States and/or the United Kingdom. Some of these geographic locations have in the past experienced natural disasters, including severe earthquakes. Earthquakes, droughts, floods, fires, disease epidemics or other natural disasters could severely disrupt our operations, and have a material adverse effect on our business, results of operations, financial condition and prospects. If a natural disaster, power outage or other event occurred that prevented us from using all or a significant portion of our facilities, that damaged critical infrastructure, such as the manufacturing facilities of our third-party contract manufacturers, or that otherwise disrupted operations, it may be difficult or, in certain cases, impossible for us to continue our business for a substantial period of time. The disaster recovery and business continuity plans we have in place currently are limited and are unlikely to prove adequate in the event of a serious disaster or similar event. We may incur substantial expenses as a result of the limited nature of our disaster recovery and business continuity plans, as well as limits on our insurance coverage, which could have a material adverse effect on our business, prospects, financial condition and results of operations.

Risks related to this offering and ownership of our common stock

An active trading market for our common stock may not develop.

Prior to this offering, there has not been a public market for our common stock. An active trading market for our common stock may not develop or be sustained following this offering. You may not be able to sell your shares quickly or at the market price if trading in our common stock is not active. The initial public offering price for the shares has been determined by negotiations between us and the representatives of the underwriters and may not be indicative of prices that will prevail in the trading market.

The market price of our common stock may be highly volatile, and you may not be able to resell your shares at or above the initial public offering price.

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

- adverse results or delays in preclinical studies or clinical trials;

- the imposition of a clinical hold on our product candidates or our inability to cause the clinical hold to be lifted;
- any delay in filing an IND or BLA for any of our product candidates and any adverse development or perceived adverse development with respect to the FDA's review of that IND or BLA;
- failure to develop successfully and commercialize our product candidates;
- the perception of limited market sizes or pricing for our product candidates;
- failure by us or our licensors to prosecute, maintain or enforce intellectual property rights covering our product candidates and processes;
- changes in laws or regulations applicable to future products;
- inability to obtain adequate product supply for our product candidates or the inability to do so at acceptable prices;
- adverse regulatory decisions;
- introduction of new products, services or technologies by our competitors;
- inability to obtain additional funding;
- failure to meet or exceed financial or operational projections we may provide to the public;
- failure to meet or exceed the financial or operational projections of the investment community;
- the perception of the pharmaceutical industry by the public, legislatures, regulators and the investment community;
- significant acquisitions, strategic partnerships, joint ventures or capital commitments by us or our competitors;
- disputes or other developments relating to proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our technologies;
- additions or departures of key scientific or management personnel;
- significant lawsuits, including patent or stockholder litigation;
- if securities or industry analysts do not publish research or reports about our business, or they issue an adverse or misleading opinion regarding our stock;
- changes in the market valuations of similar companies;
- general market or macroeconomic conditions;
- sales of our common stock by us or our stockholders in the future; and
- trading volume of our common stock.

In addition, companies trading in the stock market in general, and The Nasdaq Global Select Market in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may negatively affect the market price of our common stock, regardless of our actual operating performance.

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

Our executive officers, directors, five percent stockholders and their affiliates beneficially own approximately 80% of our voting stock and, upon closing of this offering, that same group will beneficially own approximately 66% of our outstanding voting stock (assuming no exercise of the underwriters' option to

purchase additional shares), taking into account 1,070,000 shares of common stock that certain of our existing stockholders have indicated an interest in purchasing, and have agreed to purchase, in this offering at the initial public offering price of $14.00 per share. Therefore, even after this offering, these stockholders will have the ability to influence us through their ownership positions and may be able to determine all matters requiring stockholder approval. For example, these stockholders, acting together, may be able to control elections of directors, amendments of our organizational documents, or approval of any merger, sale of assets, or other major corporate transaction. This may prevent or discourage unsolicited acquisition proposals or offers for our common stock that you may believe are in your best interest as one of our stockholders.

Participation in this offering by certain of our existing stockholders would reduce the available public float for our shares.

Certain of our existing stockholders, including one stockholder affiliated with one of our directors, have indicated an interest in purchasing, and have agreed to purchase, an aggregate of 1,070,000 shares of our common stock in this offering at the initial public offering price. After giving effect to these purchases, such stockholders would beneficially own approximately 18.4% of our outstanding common stock after this offering. This percentage would increase if any of our existing stockholders purchase additional shares of common stock in this offering. The purchase of shares in this offering by our existing stockholders will reduce the available public float for our shares because such stockholders will be restricted from selling the shares by a lock-up agreement they have entered into with our underwriters and/or by restrictions under applicable securities laws. As a result, any purchase of shares by such stockholders in this offering may reduce the liquidity of our common stock relative to what it would have been had these shares been purchased by investors that were not affiliated with us.

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

We are an "emerging growth company," as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including not being required to comply with the auditor attestation requirements of Section 404 of the Sarbanes-Oxley Act reduced disclosure obligations regarding executive compensation in this prospectus and our periodic reports and proxy statements and exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved. We could be an emerging growth company for up to five years, although circumstances could cause us to lose that status earlier, including if the market value of our common stock held by non-affiliates exceeds $700.0 million as of any June 30 before that time or if we have total annual gross revenue of $1.0 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 this prospectus and 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.

You will incur immediate and substantial dilution in the book value of your shares.

Investors purchasing shares of common stock in this offering will pay a price per share that substantially exceeds the pro forma book value per share of our tangible assets after subtracting our liabilities. As a result, investors purchasing shares of common stock in this offering will incur immediate dilution of $7.45 per share, based on the initial public offering price of $14.00 per share, and our pro forma net tangible book value as of December 31, 2014. For information on how the foregoing amounts were calculated, see "Dilution." To the extent shares are issued under outstanding options or warrants, or pursuant to the conversion of convertible debt, investors will incur further dilution. As a result of the dilution to investors purchasing shares in this offering, investors may receive significantly less than the purchase price paid in this offering, if anything, in the event of our liquidation.

Sales of a substantial number of shares of our common stock in the public market could cause our stock price to fall.

If our existing stockholders sell, or indicate an intention to sell, substantial amounts of our common stock in the public market after the lock-up and other legal restrictions on resale discussed in this prospectus lapse, the market price of our common stock could decline. Based upon the number of shares of common stock outstanding on an as-converted basis as of December 31, 2014, and including the shares of common stock issuable upon the conversion of the shares of our Series E redeemable convertible preferred stock issued in March 2015, upon the closing of this offering, we will have outstanding a total of 22,549,739 shares of common stock, assuming no exercise of the underwriters' option to purchase additional shares and no exercise of outstanding warrants and options. Of these shares, as of the date of this prospectus, approximately 221,793 shares of our common stock, plus any shares sold upon exercise of the underwriters' option to purchase additional shares, will be freely tradable, without restriction, in the public market immediately following this offering, except for any shares purchased in this offering by certain of our stockholders or held by our "affiliates" as that term is defined under Rule 144 of the Securities Act of 1933, as amended, or the Securities Act. The underwriters, however, may, in their sole discretion and under the terms of the lock-up agreements, permit our officers, directors and other stockholders who are subject to the lock-up agreements to sell shares prior to the expiration of the lock-up agreements.

The lock-up agreements pertaining to this offering will expire 180 days from the date of this prospectus. After the lock-up agreements expire, based upon the number of shares of common stock outstanding on an as-converted basis as of December 31, 2014, and including the shares of common stock issuable upon the conversion of the shares of our Series E redeemable convertible preferred stock issued in March 2015, up to an additional 16,967,946 shares of common stock will be eligible for sale in the public market, a portion of which are held by directors, executive officers and other affiliates and will be subject to Rule 144 under the Securities Act.

In addition, approximately 3,819,748 shares of common stock that are either subject to outstanding options, reserved for future issuance under our equity incentive plans or employee stock purchase plan or subject to outstanding warrants will become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules, the lock-up agreements and Rule 144 and Rule 701 under the Securities Act. If these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the market price of our common stock could decline.

After this offering, the holders of approximately 16,292,431 shares of our common stock will be entitled to rights with respect to the registration of their shares under the Securities Act, subject to the lock-up agreements described above. Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares purchased by affiliates. Any sales of securities by these stockholders could have a material adverse effect on the market price of our common stock.

Future sales and issuances of our common stock or rights to purchase common stock, including pursuant to our equity incentive plans, could result in additional dilution of the percentage ownership of our stockholders and could cause our stock price to fall.

We will need additional capital in the future to continue our planned operations. To the extent we raise additional capital by issuing equity securities, our stockholders may experience substantial dilution. We may sell common stock, convertible securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell common stock, convertible securities or other equity securities in more than one transaction, investors may be materially diluted by subsequent sales. These sales may also result in material dilution to our existing stockholders, and new investors could gain rights superior to our existing stockholders.

Pursuant to our 2015 Stock Option and Incentive Plan, or the 2015 Plan, we are authorized to grant stock options and other equity-based awards to our employees, directors and consultants. The number of shares available for future grant under the 2015 Plan will automatically increase each year on January 1, from January 1, 2016 to January 1, 2019, by the lesser of (i) 1,840,000 shares of common stock, (ii) 4% of all shares of our capital stock outstanding as of December 31 of the prior calendar year, and (iii) an amount as determined by our compensation committee of our board of directors. In addition, 227,623 shares of our common stock are reserved for future issuance pursuant to our 2015 Employee Stock Purchase Plan, or 2015 ESPP, which number of shares will automatically increase each year on January 1, from January 1, 2016 to January 1, 2019, by 1% of all shares of our capital stock outstanding as of December 31 of the prior calendar year, or such lesser number of shares as determined by the administrator of our 2015 ESPP. Currently, we plan to register the increased number of shares available for issuance under the 2015 Plan and 2015 ESPP each applicable year. If the number of shares available for future grant under the 2015 Plan and 2015 ESPP increases each year, our stockholders may experience additional dilution, which could cause our stock price to decline.

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

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

We could be subject to securities class action litigation.

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

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

Our management will have broad discretion in the application of the net proceeds from 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 the net proceeds are being used appropriately. Because of the number and variability of factors that will determine our use of the 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 harm our business. Pending their use, we may invest the net proceeds from this offering in short-term, investment-grade, interest-bearing securities. These investments may not yield a favorable return to our stockholders.

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

We have incurred substantial losses during our history, we do not expect to become profitable in the near future and we may never achieve profitability. Unused losses generally are available to be carried forward to offset future taxable income, if any, until such unused losses expire. Under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, if a corporation undergoes an "ownership change," generally defined as a greater than 50% change (by value) in its equity ownership over a three-year period, the corporation's ability to use its pre-change net operating loss carryforwards, or NOLs, and other pre-change tax attributes (such as research tax credits) to offset its post-change taxable income or taxes may be limited. We completed an analysis through September 7, 2011, and determined that on November 30, 2006 an ownership change occurred, for which we have adjusted our NOL and research and development tax credit carryforwards. We may have experienced an ownership change subsequent to September 7, 2011, and we may also experience ownership changes in the future as a result of this offering or subsequent shifts in our stock ownership, some of which may be outside of our control. As a result, our ability to use our pre-change NOLs to offset U.S. federal taxable income may be subject to limitations, which could potentially result in increased future tax liability to us. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed.

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

We have never declared or paid any cash dividends on our common stock. We anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Any return to stockholders will therefore be limited to the appreciation of their stock.

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

Our amended and restated certificate of incorporation, amended and restated bylaws and Delaware law contain or will 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, which will become effective upon the closing of this offering, 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.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, including the sections entitled "Prospectus Summary," "Risk Factors," "Management's Discussion and Analysis of Financial Condition and Results of Operations" and "Business," contains forward-looking statements that are based on our management's belief and assumptions and on information currently available to our management. Although we believe that the expectations reflected in these forward-looking statements are reasonable, these statements relate to future events or our future operational or financial performance, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Forward-looking statements in this prospectus include, but are not limited to, statements about:

- the success, cost and timing of our clinical trials, including our ongoing and planned Phase 1b/2 trials of Resolaris, and whether the results of our trials will be sufficient to support domestic or foreign regulatory approvals;
- the likelihood and timing of regulatory approvals for Resolaris and any of our other product candidates;
- our ability to identify and discover additional product candidates;
- whether our existing capital resources and the net proceeds from this offering will be sufficient to enable us to complete any particular portion of our planned clinical development of Resolaris;
- our ability to obtain, maintain, defend and enforce intellectual property rights protecting our product candidates;
- our estimates of our expenses, ongoing losses, future revenue, capital requirements and our needs for or ability to obtain additional financing;
- performance of third-party service providers and independent contractors upon whom we rely to conduct our clinical trials and to manufacture our product candidates or certain components of our product candidates;
- our ability to develop sales and marketing capabilities or to enter into strategic partnerships to develop and commercialize Resolaris or any of our other product candidates;
- the timing and success of the commercialization of Resolaris or any of our other product candidates;
- the rate and degree of market acceptance of our product candidates;
- the size and growth of the potential markets for our product candidates and our ability to serve those markets;
- regulatory developments in the United States and foreign countries;
- the success of competing therapies that are or may become available;
- our ability to attract and retain key scientific or management personnel;
- our expectations regarding the period during which we qualify as an emerging growth company under the Jumpstart Our Business Startups Act of 2012; and
- our use of the proceeds from this offering.

In some cases, you can identify forward-looking statements by terminology such as "may," "will," "should," "expects," "intends," "plans," "anticipates," "believes," "estimates," "predicts," "potential," "continue" or the negative of these terms or other comparable terminology. These statements are only predictions. You should not place undue reliance on forward-looking statements because they involve known and unknown risks, uncertainties and other factors, which are, in some cases, beyond our control and which could materially affect results. Factors that may cause actual results to differ materially from current expectations include, among other

things, those listed under "Risk Factors" and elsewhere in this prospectus. If one or more of these risks or uncertainties occur, or if our underlying assumptions prove to be incorrect, actual events or results may vary significantly from those implied or projected by the forward-looking statements. No forward-looking statement is a guarantee of future performance. You should read this prospectus and the documents that we reference in this prospectus and have filed with the Securities and Exchange Commission as exhibits to the registration statement, of which this prospectus is a part, completely and with the understanding that our actual future results may be materially different from any future results expressed or implied by these forward-looking statements.

The forward-looking statements in this prospectus represent our views as of the date of this prospectus. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so except to the extent required by applicable law. You should therefore not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this prospectus.

USE OF PROCEEDS

We estimate that the net proceeds to us from the sale of 5,360,000 shares of common stock in this offering will be approximately $66.4 million based upon the initial public offering price of $14.00 per share, and after deducting underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters' option to purchase additional shares in this offering is exercised in full, we estimate that our net proceeds will be approximately $76.9 million, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

The principal purposes of this offering are to obtain additional capital to support our operations, to establish a public market for our common stock and to facilitate our future access to the public markets. We intend to use the net proceeds from this offering as follows:

- approximately $11.0 million to fund our ongoing Phase 1b/2 clinical trial of Resolaris in adult patients with FSHD through completion of the third cohort and the initiation of up to two additional cohorts, and to conduct additional studies to evaluate the safety, tolerability and extended treatment of FSHD;
- approximately $16.1 million to fund portions of additional Phase 1b/2 clinical trials of Resolaris in early onset FSHD, LGMD and an additional indication, such as ILD;
- approximately $7.9 million to fund the initiation of potential Phase 3 or pivotal clinical trials of Resolaris in adult patients with FSHD;
- approximately $15.8 million to advance other research, discovery and development activities; and
- the remainder for working capital and other general corporate purposes, including funding the costs of operating as a public company.

In December 2011, in connection with our facility lease, we issued a $2.0 million subordinated convertible unsecured promissory note to the venture arm of our landlord, BioMed Realty, L.P. which was subsequently transferred to its affiliate, BMV Direct RE LP. The note bears interest at an annual rate of 8.0% and matures at the earlier of (i) May 2015, (ii) a liquidation event, and (iii) the closing of an initial firm commitment underwritten public offering of our common stock pursuant to a registration statement under the Securities Act, unless previously converted. At any time prior to maturity, the holder may elect to convert the principal outstanding under the promissory note into shares of our Series D redeemable convertible preferred stock at the price of $2.662 per share, and upon conversion, all accrued interest would be forgiven. We may use a portion of the proceeds from this offering to repay the principal and accrued interest under the note, equal to approximately $2.5 million as of December 31, 2014, assuming the note holder does not elect, on or prior to the date of completion of this offering, to forgive all accrued interest under the note and convert the $2.0 million in principal under the note into 751,314 shares of our Series D redeemable convertible preferred stock, which would convert into 94,455 shares of common stock upon completion of this offering, in accordance with the terms described above.

We may also use a portion of the net proceeds to in-license, acquire, or invest in additional businesses, technologies, products, or assets. Although we have no specific agreements, commitments, or understandings with respect to any in-license or acquisition, we evaluate such opportunities and engage in related discussions with other companies from time to time. As of the date of this prospectus, we cannot predict with certainty all of the particular uses for the net proceeds from this offering. The amounts and timing of our actual expenditures may vary significantly from our expectations depending upon numerous factors, including the progress of our research and development efforts, the progress of our clinical trials, our operating costs and capital expenditures and the other factors described under "Risk Factors" in this prospectus. Accordingly, we will retain the discretion to allocate the net proceeds of this offering among the identified uses described above, and we reserve the right to change the allocation of the net proceeds among the uses described above.

Pending these uses, we intend to invest the net proceeds in investment grade instruments, certificates of deposit or direct or guaranteed obligations of the U.S. government, or hold the net proceeds as cash.

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. Any future determination to pay dividends will be made at the discretion of our board of directors.

CAPITALIZATION

The following table sets forth our cash, cash equivalents and investment securities and capitalization as of December 31, 2014:

- on an actual basis;
- on a pro forma basis to give effect to (i) the filing and effectiveness of our amended and restated certificate of incorporation in March 2015, (ii) the issuance and sale of 68,166,894 shares of our Series E redeemable convertible preferred stock in March 2015 for aggregate gross proceeds of approximately $76.3 million, (iii) the conversion of all outstanding shares of our redeemable convertible preferred stock into an aggregate of 16,279,859 shares of common stock immediately prior to the completion of this offering, and the resultant reclassification of our redeemable convertible preferred stock to stockholders' equity (deficit), (iv) the adjustment of our outstanding warrants to purchase redeemable convertible preferred stock into warrants to purchase 25,970 shares of our common stock, and the resultant reclassification of our preferred stock warrant liabilities to additional paid-in capital, a component of stockholders' equity (deficit) and (v) our repayment in cash, upon the completion of this offering, of approximately $2.5 million in principal and accrued interest as of December 31, 2014 under a convertible promissory note issued to an affiliate of our landlord, assuming the note holder does not elect, on or prior to the date of completion of this offering, to forgive all accrued interest under the note and convert the $2.0 million in principal under the note into 751,314 shares of our Series D redeemable convertible preferred stock, which would convert into 94,455 shares of common stock upon the completion of this offering; and
- on a pro forma as adjusted basis to give further effect to (i) the filing and effectiveness of our amended and restated certificate of incorporation and the retirement of 141,654,309 shares of our redeemable convertible preferred stock following the conversion of all outstanding shares of our redeemable convertible preferred stock and (ii) our sale in this offering of 5,360,000 shares of common stock at the initial public offering price of $14.00 per share, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us.

You should read the following table together with "Management's Discussion and Analysis of Financial Condition and Results of Operations," "Description of Capital Stock," and the consolidated financial statements and related notes appearing elsewhere in this prospectus.

	As of December 31, 2014		
	Actual	Pro Forma	Pro Forma As Adjusted
	(in thousands, except share and per share data)		
Cash, cash equivalents and investment securities	$15,853	$ 89,647	$ 157,033
Capitalization:			
Commercial bank debt (including current portion)	$ 8,276	$ 8,276	$ 8,276
Convertible promissory notes (including accrued interest)	2,485	—	—
Warrant liabilities	319	—	—
Redeemable convertible preferred stock, $0.001 par value; 75,772,871 shares authorized and 73,487,415 shares issued and outstanding, actual; 143,939,765 shares authorized and no shares issued and outstanding, pro forma; 2,285,456 shares authorized and no shares issued and outstanding, pro forma as adjusted	95,619	—	—

	As of December 31, 2014		
	Actual	Pro Forma	Pro Forma As Adjusted
	(in thousands, except share and per share data)		
Stockholders' equity (deficit):			
Preferred stock, $0.001 par value; no shares authorized, issued and outstanding, actual and pro forma; 5,000,000 shares authorized and no shares issued and outstanding, pro forma as adjusted	—	—	—
Common stock, $0.001 par value; 95,500,000 shares authorized and 909,880 shares issued and outstanding, actual; 185,000,000 shares authorized and 17,189,739 shares issued and outstanding, pro forma; 150,000,000 shares authorized and 22,549,739 shares issued and outstanding, pro forma as adjusted	1	17	23
Additional paid-in capital	19,209	191,410	257,791
Stockholder note receivable	(69)	(69)	(69)
Accumulated deficit	(110,151)	(110,151)	(110,151)
Total stockholders' equity (deficit)	(91,010)	81,207	147,594
Total capitalization	$ 15,689	$ 89,483	$ 155,870

The information set forth in the table excludes:

- 1,514,471 shares of common stock issuable upon the exercise of stock options outstanding as of December 31, 2014 at a weighted average exercise price of $4.60 per share;
- 25,970 shares of common stock issuable upon the exercise of warrants outstanding as of December 31, 2014 at a weighted average exercise price of $14.44 per share of common stock, which warrants prior to the completion of this offering are exercisable to purchase redeemable convertible preferred stock;
- the issuance of 119,840 shares of common stock to The Scripps Research Institute on March 31, 2015;
- 639,619 shares of common stock issuable upon the exercise of stock options granted to employees, directors and consultants subsequent to December 31, 2014 at a weighted average exercise price of $9.15 per share;
- 1,574,566 shares of common stock reserved for future issuance under the 2015 Plan, options to purchase 377,158 shares of which will be issued in connection with this offering at an exercise price equal to the initial public offering price, and which 2015 Plan became effective upon the effectiveness of the registration statement of which this prospectus is a part; and
- 227,623 shares of common stock reserved for issuance under our 2015 ESPP, which became effective upon effectiveness of the registration statement of which this prospectus is a part.

DILUTION

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

As of December 31, 2014, we had a historical net tangible book deficit of $(91.0) million, or $(100.02) per share of common stock, based on 909,880 shares of common stock outstanding at December 31, 2014. Our historical net tangible book value per share represents the amount of our total tangible assets less total liabilities and redeemable convertible preferred stock, divided by the total number of shares of common stock outstanding as of December 31, 2014.

On a pro forma basis, after giving effect to (i) the issuance and sale of 68,166,894 shares of our Series E redeemable convertible preferred stock in March 2015 for aggregate gross proceeds of approximately $76.3 million, (ii) the conversion of all outstanding shares of our redeemable convertible preferred stock into an aggregate of 16,279,859 shares of common stock immediately prior to the completion of this offering, and the resultant reclassification of our redeemable convertible preferred stock to stockholders' equity (deficit) and (iii) the adjustment of our outstanding warrants to purchase redeemable convertible preferred stock into warrants to purchase 25,970 shares of our common stock, and the resultant reclassification of our preferred stock warrant liabilities to additional paid-in capital, a component of stockholders' equity (deficit), our pro forma net tangible book value as of December 31, 2014 would have been approximately $81.2 million, or approximately $4.72 per share of our common stock.

After giving further effect to our sale of 5,360,000 shares of common stock in this offering at the initial public offering price of $14.00 per share, and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma as adjusted net tangible book value as of December 31, 2014 would have been approximately $147.6 million, or approximately $6.55 per share. This amount represents an immediate increase in pro forma net tangible book value of $1.83 per share to our existing stockholders and an immediate dilution in pro forma net tangible book value of approximately $7.45 per share to new investors participating in this offering. The following table illustrates this dilution:

Initial public offering price per share		$14.00
Historical net tangible book deficit per share	$(100.02)	
Pro forma increase in historical net tangible book deficit per share	104.74	
Pro forma net tangible book value per share	4.72	
Increase in pro forma net tangible book value per share attributable to investors participating in this offering	1.83	
Pro forma as adjusted net tangible book value per share after this offering		6.55
Dilution per share to new investors participating in this offering		$ 7.45

If the underwriters exercise their option to purchase additional shares of common stock in this offering in full, the pro forma as adjusted net tangible book value would be $6.77 per share, and the dilution in pro forma net tangible book value per share to investors in this offering would be $7.23 per share.

The following table summarizes, on a pro forma basis, as of December 31, 2014, the difference between the number of shares of common stock purchased from us, the total consideration paid to us and the average price per share paid by existing stockholders and by new investors in this offering at the initial public offering price of $14.00 per share, before deducting underwriting discounts and commissions and estimated offering expenses payable by us.

	Shares Purchased		Total Consideration		Average Price Per Share
	Number	Percent	Amount	Percent	
	(in thousands, except share and per share amounts)				
Existing stockholders	17,189,739	76%	$172,236	70%	$ 10.02
New investors	5,360,000	24	75,040	30	14.00
Total	22,549,739	100%	$247,276	100%	

The above discussion and tables are based on 17,189,739 shares of common stock issued and outstanding as of December 31, 2014, which includes the conversion of all outstanding shares of redeemable convertible preferred stock, including the shares of our Series E redeemable convertible preferred stock issued in March 2015, into an aggregate of 16,279,859 shares of common stock immediately prior to the completion of this offering and excludes:

- 1,514,471 shares of common stock issuable upon the exercise of stock options outstanding as of December 31, 2014 at a weighted average exercise price of $4.60 per share;
- 25,970 shares of common stock issuable upon the exercise of warrants outstanding as of December 31, 2014 at a weighted average exercise price of $14.44 per share of common stock, which warrants prior to the completion of this offering are exercisable to purchase redeemable convertible preferred stock;
- the issuance of 119,840 shares of common stock to The Scripps Research Institute on March 31, 2015;
- 639,619 shares of common stock issuable upon the exercise of stock options granted to employees, directors and consultants subsequent to December 31, 2014 at a weighted average exercise price of $9.15 per share;
- 94,455 shares of common stock issuable upon the conversion of 751,314 shares of Series D redeemable convertible preferred stock that may be issued under a convertible promissory note issued to an affiliate of our landlord, if the noteholder elects to convert the note in accordance with its terms;
- 1,574,566 shares of common stock reserved for future issuance under the 2015 Plan, options to purchase 377,158 shares of which will be issued in connection with this offering at an exercise price equal to the initial public offering price, and which 2015 Plan became effective upon the effectiveness of the registration statement of which this prospectus is a part; and
- 227,623 shares of common stock reserved for issuance under our 2015 ESPP, which became effective upon effectiveness of the registration statement of which this prospectus is a part.

Certain of our existing stockholders, including a stockholder affiliated with one of our directors, have indicated an interest in purchasing, and have agreed to purchase, an aggregate of 1,070,000 shares of our common stock in this offering at the initial public offering price. The underwriting discount for the shares sold to these investors in the offering will be the same as the underwriting discount for the shares sold to the public. The foregoing discussion and tables do not reflect any purchases in this offering by these investors.

To the extent that outstanding options and warrants are exercised, or the holder of our convertible promissory note elects to convert the note into shares of our Series D redeemable convertible preferred stock, you will experience further dilution. In addition, we may choose to raise additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that additional capital is raised through the sale of equity or convertible debt securities, the issuance of these securities may result in further dilution to our stockholders.

SELECTED CONSOLIDATED FINANCIAL DATA

You should read the following selected historical consolidated financial data below together with "Management's Discussion and Analysis of Financial Condition and Results of Operations" and the financial statements, related notes and other financial information included elsewhere in this prospectus. The selected consolidated financial data in this section are not intended to replace the financial statements and are qualified in their entirety by the consolidated financial statements and related notes included elsewhere in this prospectus.

The selected consolidated statement of operations data for the years ended December 31, 2013 and 2014 and the selected consolidated balance sheet data as of December 31, 2014 are derived from our audited consolidated financial statements appearing elsewhere in this prospectus. Our historical results are not necessarily indicative of results that may be expected in the future.

	Years Ended December 31,	
	2013	2014
	(in thousands, except share and per share data)	
Statements of Operations Data:		
Operating expenses:		
Research and development	$ 13,832	$ 16,777
General and administrative	5,710	6,777
Total operating expenses	19,542	23,554
Loss from operations	(19,542)	(23,554)
Other income (expense)	(472)	(796)
Net loss	(20,014)	(24,350)
Accretion to redemption value of redeemable convertible preferred stock	(1,637)	(416)
Net loss attributable to common stockholders	$ (21,651)	$ (24,766)
Net loss per share attributable to common stockholders, basic and diluted (1)	$ (28.39)	$ (29.69)
Weighted average shares outstanding, basic and diluted (1)	762,761	834,221
Pro forma net loss per share attributable to common stockholders, basic and diluted (unaudited) (1)		$ (2.42)
Pro forma weighted average shares outstanding, basic and diluted (unaudited) (1)		10,073,089

(1) See Note 2 to our audited consolidated financial statements included elsewhere in this prospectus for an explanation of the method used to calculate the historical and pro forma net loss per share, basic and diluted, and the number of shares used in the computation of the per share amounts.

	As of December 31,	
	2013	2014
	(in thousands)	
Consolidated Balance Sheet Data:		
Cash, cash equivalents and investment securities	$ 36,457	$ 15,853
Total assets	39,786	20,644
Preferred stock warrant liabilities	207	319
Convertible promissory note	2,000	2,000
Working capital	31,814	6,396
Commercial bank debt, net of current portion	4,158	5,142
Redeemable convertible preferred stock	93,165	95,619
Accumulated deficit	(85,801)	(110,151)
Noncontrolling interest	2,414	—
Total stockholders' deficit	(66,082)	(91,010)

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

You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and related notes and other financial information appearing elsewhere in this prospectus. Some of the information contained in this discussion and analysis or set forth elsewhere in this prospectus, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk Factors" section of this prospectus, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We engage in the discovery and clinical development of innovative medicines for patients suffering from severe, rare diseases using our knowledge of Physiocrine biology, a newly discovered set of physiological modulators. We have discovered approximately 300 Physiocrines, a class of naturally occurring human proteins that we believe promote homeostasis, a fundamental process of restoring stressed or diseased tissue to a healthier state. By leveraging our discovery engine and our knowledge of rare diseases, we aim to build a proprietary pipeline of novel product candidates with the potential to treat severe, rare diseases characterized by immune dysregulation. We plan to independently commercialize our Physiocrine-based therapeutics.

In the first quarter of 2014, we completed a double-blind, placebo-controlled Phase 1 clinical trial of Resolaris, our lead development candidate from our discovery engine, in which we assessed its safety and tolerability in 32 healthy subjects. Resolaris was shown to be well tolerated at all doses tested, and no serious adverse events were reported. Based on the favorable clinical safety, tolerability, pharmacokinetic and immunogenicity profile of Resolaris in this trial, we decided to advance Resolaris into clinical trials of patients affected by rare myopathies with an immune component. We are currently conducting a multi-national exploratory Phase 1b/2 clinical trial of Resolaris in the European Union in adult patients with facioscapulohumeral muscular dystrophy, or FSHD, a severe, rare genetic myopathy in which immune cells invade diseased muscle, and for which there are no approved treatments. Subject to our interactions with regulatory authorities and patient enrollment in accordance with our clinical development plans, we expect to report initial results from this clinical trial in the fourth quarter of 2015 or early 2016.

Since our inception in 2005, we have devoted substantially all of our resources to the therapeutic application of Physiocrines, including the preclinical development of and clinical trials for Resolaris, the creation, licensing and protection of related intellectual property and the provision of general and administrative support for these operations. We have not generated any revenue from product sales and, to date, have funded our operations primarily with the aggregate proceeds of $171.9 million from the private placement of redeemable convertible preferred stock and convertible promissory notes, $10.0 million of commercial bank debt and a $2.0 million convertible promissory note issued to our landlord.

We have never been profitable and have incurred net losses in each annual and quarterly period since our inception. Our net losses were $20.0 million and $24.4 million for the years ended December 31, 2013 and 2014, respectively. As of December 31, 2014, we had an accumulated deficit of $110.2 million.

Substantially all of our net losses resulted from costs incurred in connection with our development of and clinical trials for Resolaris, our other research and development programs and from general and administrative costs associated with our operations. We expect to continue to incur significant expenses and increasing operating losses for the foreseeable future, at least until we apply for and receive regulatory approval for Resolaris or another product candidate and generate substantial revenues from its commercialization, if ever. Our

net losses may fluctuate significantly from quarter to quarter and year to year, depending on the nature and extent of our research and development expenses and clinical trials. We expect our expenses will increase substantially in connection with our ongoing activities as we:

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

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

Financial Operations Overview

Organization and Business; Principles of Consolidation and Affiliates

We conduct substantially all of our activities through aTyr Pharma, Inc., a Delaware corporation, at our facility in San Diego, California. aTyr Pharma, Inc. was incorporated in the state of Delaware in September 2005. The consolidated financial statements include the accounts of aTyr Pharma, Inc., its 98% majority-owned subsidiary in Hong Kong, Pangu BioPharma Limited, and six variable interest entities, which we refer to as the Affiliates.

In October and November 2011, we established the Affiliates to perform research and development for specified programs. In April 2012, we purchased preferred and common stock of each Affiliate and subsequently issued those shares to each of our stockholders in the form of dividends, in proportion to their relative holdings of aTyr Pharma, Inc. in order to effectuate the spin-out of the Affiliates into stand-alone entities. We entered into nonexclusive license agreements allowing each Affiliate to utilize certain intellectual property owned by us. We also entered into research and development services agreements in our therapeutic program area of interest covered by the respective nonexclusive license agreement with each Affiliate. The working capital of the Affiliates was primarily provided by amounts borrowed from us under convertible promissory note agreements. The Affiliates were not capitalized with sufficient equity to finance their operations and were each therefore considered a variable interest entity, or VIE. In May 2012, the Affiliates commenced operations. The Affiliates had no employees and substantially all of their expenses related to the services provided to them by us, and the expenses related to services provided by us have been eliminated in consolidation. The liquidation preferences underlying the preferred stock issued by the Affiliates and the convertible promissory notes issued by the

Affiliates to us effectively protected stockholders of the Affiliates from absorbing the losses of the Affiliates and, as a result, no losses were allocated to these noncontrolling interests and such losses are included in our consolidated net loss. None of the related parties to the Affiliates individually had the power and benefits to control the Affiliates. Because we were the related party that was most closely associated with each VIE, we have consolidated the six Affiliates for financial reporting purposes.

In the fourth quarter of 2014, the board of directors and stockholders of each of the Affiliates approved the dissolution of each applicable Affiliate in accordance with the laws of its respective jurisdiction of organization. In connection with the dissolution of the Affiliates, the license and operating agreements by and between aTyr Pharma, Inc. and each Affiliate were terminated. Our consolidated financial statements for periods after the effectiveness of the dissolution of the Affiliates will no longer include a noncontrolling interest, and the operating activities that the Affiliates performed prior to dissolution will be continued by aTyr Pharma, Inc.

Research and Development Expenses

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

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

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

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

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 program, we are unable to estimate with any certainty the costs we will incur or the timelines we will require in the continued development of Resolaris and any other product candidates that we may develop. Clinical and preclinical development timelines, the probability of success and development costs can differ materially from expectations. We anticipate that we will make determinations as to which product candidates to pursue and how much funding to direct to each product candidate on an ongoing basis in response to the results of ongoing and future

preclinical studies and clinical trials, regulatory developments and our ongoing assessments as to each product candidate's commercial potential. In addition, we cannot forecast which product candidates may be subject to future collaborations, when such arrangements will be secured, if at all, and to what degree such arrangements would affect our development plans and capital requirements.

General and Administrative Expenses

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

We anticipate that our general and administrative expenses will substantially increase for the foreseeable future as we increase our headcount to support the continued development of our product candidates and the increased costs of operating as a public company, including expenses related to services associated with maintaining compliance with NASDAQ listing rules and the Securities and Exchange Commission, or SEC, requirements, insurance and investor relations costs. These increases will likely include increased costs related to the hiring of additional personnel and fees to outside consultants, lawyers and accountants, among other expenses.

Other Income (Expense)

Other income (expense) primarily consists of interest income and expense and changes in the fair value of preferred stock warrant liabilities related to warrants we issued in connection with commercial bank debt. We do not expect any further fair value adjustments for these warrants subsequent to our initial public offering, when these liabilities will be reclassified to additional paid-in capital.

Critical Accounting Policies and Significant Judgments and Estimates

Our management's discussion and analysis of financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States, or GAAP. The preparation of these consolidated financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities as of the date of the consolidated financial statements, as well as the reported expenses during the reporting periods. We monitor and analyze these items for changes in facts and circumstances, and material changes in these estimates could occur in the future. We base our estimates on our historical experience and on various other factors we believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Changes in estimates are reflected in reported results for the period in which they become known. Actual results may differ materially from these estimates under different assumptions or conditions.

While our significant accounting policies are more fully described in the notes to our consolidated financial statements appearing elsewhere in this prospectus, we believe the following accounting policies related to research and development expense accruals and stock-based compensation are most critical to understanding and evaluating our reported consolidated financial results.

Research and Development Expense Accruals

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued expenses. This process involves reviewing open contracts and purchase orders, communicating with our

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

We currently rely on third parties for the clinical development of Resolaris and the manufacture of Resolaris to support our ongoing Phase 1b/2 clinical trial in adult patients with FSHD. We pay these third parties, including consultants, CROs, manufacturers and other service providers, pursuant to contractual arrangements, which may include provisions for time and materials-based payments, project-based fees and milestone payments. We base our accrual for these expenses on our estimates of the services received and efforts expended pursuant to our contractual arrangements. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our service providers will exceed the level of services provided and result in a prepayment of the clinical expense. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical milestones. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepaid accordingly.

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

Stock-Based Compensation

Stock-based compensation expense represents the grant date fair value of employee stock option grants recognized as expense over the requisite service period of the awards (usually the vesting period) on a straight-line basis, net of estimated forfeitures. For stock option grants with performance-based milestones, the expense is recorded over the service period after the achievement of the milestone is probable or the performance condition is achieved. We estimate the fair value of stock option grants using the Black-Scholes option pricing model. The Black-Scholes option pricing model requires the input of subjective assumptions, including the risk-free interest rate, the expected dividend yield of our common stock, the expected volatility of the price of our common stock, the expected term of the option and the fair value of our common stock. These estimates involve inherent uncertainties and the application of management's judgment. If factors change and different assumptions are used, our stock-based compensation expense could be materially different in the future. See Note 7 to our consolidated financial statements included elsewhere in this prospectus for information concerning certain of the specific assumptions we used in applying the Black-Scholes option pricing model to determine the estimated fair value of our stock options granted in 2013 and 2014.

The following table summarizes information related to stock options we granted from December 6, 2013 through the date of this prospectus:

Grant Date	Number of Common Shares Underlying Options Granted	Exercise Price per Common Share	Estimated Fair Value per Common Share	Reassessed Fair Value per Common Share
December 6, 2013	7,165	$ 4.06	$ 4.06	$ 4.06
March 5, 2014	320,553	4.06	4.06	6.76
July 10, 2014	259,198	4.06	4.06	13.12
October 10, 2014	76,827	17.74	17.74	N/A
October 24, 2014	96,840	17.74	17.74	N/A
March 31, 2015	287,708	9.15	9.15	N/A
April 2, 2015	12,572	9.15	9.15	N/A
April 17, 2015	282,868	9.15	9.15	N/A
April 25, 2015	56,471	9.15	9.15	N/A

In addition, on April 17, 2015, we approved options to purchase an aggregate of 377,158 shares of our common stock for our executive management team, which options will be issued in connection with this offering at an exercise price equal to the initial public offering price of our common stock.

The following table summarizes the stock-based compensation expense recognized in our consolidated financial statements:

	Years Ended December 31,	
	2013	2014
	(in thousands)	
Research and development	$ 96	$ 527
General and administrative	59	1,264
Total stock-based compensation expense	$155	$1,791

As of December 31, 2014, the unrecognized stock-based compensation expense related to outstanding employee stock options was $8.0 million and is expected to be recognized as expense over a weighted average period of approximately 4.9 years. The intrinsic value of all outstanding stock options as of December 31, 2014 was approximately $14.9 million, based on the initial public offering price of $14.00 per share, of which approximately $5.0 million related to vested options and approximately $9.9 million related to unvested options.

Determination of the Fair Value of Common Stock

We are required to estimate the fair value of the common stock underlying our stock-based awards when performing fair value calculations, which is the most subjective input into the Black-Scholes option pricing model. The fair value of the common stock underlying our stock-based awards was determined on each grant date by our board of directors, taking into account input from management and our most recent independent third-party valuations. All options to purchase shares of our common stock are intended to be granted with an exercise price per share no less than the fair value per share of our common stock underlying those options on the date of grant, based on the information known to us on the date of grant. In the absence of a public trading market for our common stock, on each grant date we develop an estimate of the fair value of our common stock in order to determine an exercise price for the option grants. Our determinations of the fair value of our common stock were made using methodologies, approaches and assumptions consistent with the American Institute of Certified Public Accountants *Audit and Accounting Practice Aid Series: Valuation of Privately Held Company Equity Securities Issued as Compensation*, or the Practice Aid.

Our board of directors considered various objective and subjective factors, along with input from management, to determine the fair value of our common stock, including:

- contemporaneous valuations of our common stock performed by independent third-party valuation specialists;
- our stage of development and business strategy, including the status of research and development efforts of our product candidates, and the material risks related to our business and industry;
- our results of operations and financial position, including our levels of available capital resources;
- the valuation of publicly traded companies in the life sciences and biotechnology sectors, as well as recently completed mergers and acquisitions of peer companies;
- the lack of marketability of our common stock as a private company;
- the prices of our redeemable convertible preferred stock sold to investors in arm's length transactions and the rights, preferences, and privileges of our redeemable convertible preferred stock relative to those of our common stock;
- the likelihood of achieving a liquidity event for the holders of our common stock, such as an initial public offering or a sale of our company, given prevailing market conditions;
- trends and developments in our industry;
- external market conditions affecting the life sciences and biotechnology industry sectors; and
- the composition of, and changes to, our management team and board of directors.

Common Stock Valuation Methodologies and Methods Used to Allocate our Enterprise Value to Classes of Securities

Our valuations were prepared in accordance with the guidelines in the Practice Aid, which prescribes several valuation approaches for setting the value of an enterprise, such as the cost, income and market approaches, and various methodologies for allocating the value of an enterprise to its common stock. The cost approach establishes the value of an enterprise based on the cost of reproducing or replacing the property less depreciation and functional or economic obsolescence, if present. The income approach establishes the value of an enterprise based on the present value of future cash flows that are reasonably reflective of our company's future operations, discounting to the present value with an appropriate risk adjusted discount rate or capitalization rate. The market approach is based on the assumption that the value of an asset is equal to the value of a substitute asset with the same characteristics. Each valuation methodology was considered in our valuations.

The various methods for allocating the enterprise value across our classes and series of capital stock to determine the fair value of our common stock in accordance with the Practice Aid include the following:

- *Current Value Method.* Under the current value method, once the fair value of the enterprise is established, the value is allocated to the various series of preferred and common stock based on their respective seniority, liquidation preferences or conversion values, whichever is greatest.
- *Option Pricing Method, or OPM.* Under the OPM, shares are valued by creating a series of call options with exercise prices based on the liquidation preferences and conversion terms of each equity class. The values of the preferred and common stock are inferred by analyzing these options.
- *Probability-Weighted Expected Return Method, or PWERM.* The PWERM is a scenario-based analysis that estimates the value per share based on the probability-weighted present value of expected future investment returns, considering each of the possible outcomes available to us, as well as the economic and control rights of each share class.

There are significant judgments and estimates inherent in the determination of the fair value of our common stock. These judgments and estimates include assumptions regarding our future operating performance, the time to completing an initial public offering or other liquidity event and the determination of the appropriate valuation methods. If we had made different assumptions, our stock-based compensation expense, net loss and net loss per common share could have been significantly different.

In accordance with the Practice Aid, we considered the various methods described above to determine our enterprise value and for allocating the enterprise value across our classes and series of capital stock to determine the fair value of our common stock at each valuation date.

Our valuations used to determine the exercise price of our December 2013 and March 2014 stock option grants utilized each of the cost and market approaches to determine our enterprise value and the enterprise value was allocated based on both the current value method and the OPM. Our valuations used to determine the exercise price of our July 2014 option grants utilized the cost and market approaches to determine our enterprise value and the enterprise value was allocated based on both the current value method and the OPM. We believed that the OPM and current value method were the most appropriate given the expectation of various potential liquidity outcomes and the difficulty of selecting and supporting appropriate enterprise values given our early stage of development. Our valuation effective September 30, 2014 was used to determine the exercise price of our stock option grants in October 2014 and utilized both the income and market approaches to determine our enterprise value, and the enterprise value was allocated based on the PWERM. We transitioned to the PWERM once we initiated our initial public offering process because we then had greater clarity as to our potential future liquidity events.

Retrospective Reassessment of Fair Value

As part of the preparation of the financial statements necessary for inclusion in the registration statement related to this offering, we reassessed for financial reporting purposes, on a retrospective basis, the fair value of our common stock for each stock option noted in the table above granted between October 1, 2013 and September 30, 2014. For purposes of this reassessment, we evaluated our original inputs and the methodologies used to determine our enterprise value and the methods we used to allocate enterprise value. In consideration of our decision to pursue an initial public offering in the third quarter of 2014, we determined to exclude the impact of the current value method from our determination of the fair value of our common stock for option grants made in 2014. We reassessed the fair value of our common stock for stock options granted on March 5, 2014 from $4.06 per share to $6.76 per share, using a straight-line method between the fair value of our common stock of $4.06 per share on December 31, 2013 and the fair value of our common stock of $8.51 per share on May 31, 2014, because we did not identify any significant internal or external value-generating events between the December 31, 2013 and May 31, 2014 valuation dates. The May 31, 2014 contemporaneous valuation, which was performed by an independent third-party valuation specialist, used the OPM and did not use the current value method.

We reassessed the fair value of our common stock for stock options granted on July 10, 2014 from $4.06 per share to $13.12 per share, using a straight-line method between the fair value of our common stock of $8.51 per share on May 31, 2014 and the fair value of our common stock of $17.74 per share on September 30, 2014, because we did not identify any significant internal or external value-generating events between the May 31, 2014 and September 30, 2014 valuation dates.

Common Stock Valuation as of December 31, 2014

The fair value of our common stock as of December 31, 2014 was $11.77 per share, a decrease of $5.97 per share from $17.74 per share as of September 30, 2014. The December 31, 2014 value was determined on substantially the same basis as our September 30, 2014 valuation. The decrease was driven primarily by our consideration of the pre-money valuation expected in our Series E financing, and also impacted by updated assumptions regarding the increased probability we complete an initial public offering in the near-term and certain

other assumptions regarding the timing, value and probability of other scenarios. In March 2015, we sold Series E redeemable convertible preferred stock to predominantly new investors at a purchase price of $1.119 per share, or $8.90 per share on an as-converted basis.

Common Stock Valuation as of March 31, 2015, March 2015 Option Grants and April 2015 Option Grants

The fair value of our common stock as of March 31, 2015 was $9.15 per share, a decrease of $2.62 per share from $11.77 per share as of December 31, 2014. The March 31, 2015 value was determined on substantially the same basis as our December 31, 2014 valuation, with the exception of updated assumptions regarding the increased probability that an initial public offering would be completed in the near-term and certain other assumptions regarding the timing, value and probability of other scenarios in the event a near-term initial public offering did not occur. In addition, the model was updated to "backsolve" for the $1.119 price paid by investors in the Series E financing and the probability that holders of Series E preferred stock would receive 0.10329 shares of common stock for each share of Series E preferred stock upon conversion in a qualified initial public offering, resulting in an effective price paid by the Series E investors of approximately $1.362 per share, or $10.83 per share on an as-converted basis. The primary driver of the decrease in the fair value of our common stock was our consideration of the final terms of our Series E financing, including the effective purchase price of our Series E preferred stock described above, which were negotiated at arms' length between us and the third-party Series E investors and were therefore considered by our board of directors to be the most appropriate indication of fair value of our common stock at the time of the March 2015 option grants. The $9.15 per share fair value of our common stock was utilized for the March 2015 option grants and also applied to the April 2015 option grants as our board of directors concluded no significant internal or external value-generating events had taken place between the March 31, 2015 valuation report and the April 2015 grant dates.

Following the completion of this offering, our board of directors will determine the fair value of our common stock based on its closing price as reported on the date of grant on the primary stock exchange on which our common stock is traded.

Other Company Information

Net Operating Loss and Research and Development Tax Credit Carryforwards

As of December 31, 2014, we had approximately $47.8 million, $49.8 million, and $5.4 million of net operating loss, or NOL, carryforwards for federal, state, and foreign purposes, respectively, available to offset future taxable income. The federal and state net operating loss carryforwards begin to expire in 2025 and 2016, respectively. The foreign net operating losses carry over indefinitely. As of December 31, 2014, we had federal and state research and development credit carryforwards of approximately $1.4 million, which begin to expire in 2026 for federal purposes and carry over indefinitely for state purposes.

Utilization of the domestic NOL and research and development credit carryforwards may be subject to a substantial annual limitation due to ownership change limitations that may have occurred or that could occur in the future, as required by Section 382 and 383 of the Internal Revenue Code of 1986, as amended, or the Code, as well as similar state and foreign provisions. These ownership changes may limit the amount of NOL and research and development credit carryforwards that can be utilized annually to offset future taxable income and tax, respectively. In general, an "ownership change" as defined by Section 382 of the Code results from a transaction or series of transactions over a three-year period resulting in an ownership change of more than 50% of the outstanding stock of a company by certain stockholders. Since our formation, we have raised capital through the issuance of capital stock on several occasions which 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 additional ownership change in the future.

Upon the occurrence of an ownership change under Section 382 as outlined above, utilization of the NOL and research and development credit carryforwards become subject to an annual limitation under Section 382 of

the Code, which is determined by first multiplying the value of our outstanding stock at the time of the ownership change by the applicable long-term, tax-exempt rate, which could be subject to additional adjustments. Any limitation may result in expiration of a portion of the NOL or research and development credit carryforwards before utilization. We completed an analysis through September 7, 2011, determined that an ownership change occurred on November 30, 2006, and adjusted our NOL and $15,000 of research and development tax credit carryforwards accordingly. Ownership changes that may have occurred subsequent to September 7, 2011, and future ownership changes, including any ownership changes resulting from this offering, may further limit our ability to utilize our remaining tax attributes.

Emerging Growth Company

On April 5, 2012, the Jumpstart Our Business Startups Act of 2012, or the JOBS Act, was enacted. Section 107 of the JOBS Act provides that an "emerging growth company" can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act of 1933, or the Securities Act, for complying with new or revised accounting standards. In other words, an "emerging growth company" can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this extended transition period and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for other public companies.

We intend to take advantage of the reduced reporting requirements and to rely on certain other exemptions provided by the JOBS Act. Subject to certain conditions set forth in the JOBS Act, as an "emerging growth company," the exemptions that we may rely on include, without limitation, exemptions from: (i) providing an auditor's attestation report on our system of internal controls over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act and (ii) complying with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements, known as the auditor discussion and analysis.

We will remain an "emerging growth company" until the earliest of (i) the last day of the fiscal year in which we have total annual gross revenues of $1 billion or more, (ii) the last day of our fiscal year following the fifth anniversary of the date of the completion of this offering, (iii) the date on which we have issued more than $1 billion in non-convertible debt during the previous three years or (iv) the date on which we are deemed to be a large accelerated filer under the rules of the SEC.

Results of Operations

Comparison of the Years Ended December 31, 2013 and 2014

The following table summarizes our results of operations for the years ended December 31, 2013 and 2014:

	Years Ended December 31,		Increase / (Decrease)
	2013	2014	
	(in thousands)		
Research and development expenses	$13,832	$16,777	$ 2,945
General and administrative expenses	5,710	6,777	1,067
Other income (expense)	(472)	(796)	324

Research and development expenses. Research and development expenses were $13.8 million and $16.8 million for the years ended December 31, 2013 and 2014, respectively. The increase of $2.9 million was due primarily to a $2.2 million increase in regulatory and clinical activities related to the completion of our Phase 1 clinical trial of Resolaris and the initiation of our multi-national Phase 1b/2 clinical trial of Resolaris in adult

patients with FSHD in the European Union, a $1.5 million increase related to compensation expenses (including stock-based compensation) as a result of increased headcount across our research and development organization and a $1.0 million increase in pre-clinical expenditures, facilities and other research costs. These increases were offset by a decrease of $1.8 million related to the timing of manufacturing costs incurred in support of various Resolaris clinical development activities.

General and administrative expenses. General and administrative expenses were $5.7 million and $6.8 million for the years ended December 31, 2013 and 2014, respectively. The increase of $1.1 million was due primarily to a $1.2 million increase in personnel costs resulting from increased headcount in our executive leadership team and stock-based compensation and a $0.2 million increase in travel and facility-related expenses, offset by a decrease of $0.3 million related to market studies that did not recur in 2014.

Other income (expense). Other income (expense) was $(0.5) million and $(0.8) million for the years ended December 31, 2013 and 2014, respectively. The increase of $0.3 million in other expense was primarily the result of additional interest expense related to the $5.0 million we borrowed under a loan agreement with Silicon Valley Bank in June 2014 and a $36,000 decrease in other expense related to decreases in the fair value of outstanding warrant liabilities as the underlying preferred stock fair value decreased.

Liquidity and Capital Resources

We have incurred losses and negative cash flows from operations since our inception. As of December 31, 2014, we had an accumulated deficit of $110.2 million and we expect to continue to incur net losses for the foreseeable future. As of December 31, 2014, we had cash, cash equivalents and investments of $15.9 million. We believe that our existing cash, cash equivalents and investments as of December 31, 2014, together with the net proceeds from this offering and the net proceeds from our Series E redeemable convertible preferred stock financing in March 2015, will be sufficient to meet our anticipated cash requirements through at least the next 12 months.

Sources of Liquidity

From our inception through December 31, 2014, we have funded our operations primarily with aggregate proceeds of $95.6 million from the private placement of redeemable convertible preferred stock and convertible promissory notes, $10.0 million of commercial bank debt and a $2.0 million convertible promissory note issued to our landlord. In March 2015, we issued an aggregate of 68,166,894 shares of Series E redeemable convertible preferred stock at a purchase price of $1.119 per share, for aggregate proceeds of $76.3 million.

Debt Financing

In each of July 2013 and June 2014, we borrowed $5.0 million under a $10.0 million loan and security agreement with Silicon Valley Bank, or SVB, which we refer to as the SVB Loan. Beginning in July 2014, we are obligated to make equal payments of principal and interest through the maturity date of June 1, 2017. The interest rate is a per annum fixed rate of 5.0% and 5.88% for the $5.0 million drawn in each of July 2013 and June 2014, respectively. The final payment due in June 2017 includes an additional fee of $0.5 million. The SVB Loan is collateralized by all of our assets, other than our intellectual property, and contains customary affirmative and negative covenants, reporting requirements and events of default. In connection with the SVB Loan, we issued a warrant to purchase 118,624 shares of Series D redeemable convertible preferred stock at an exercise price of $2.529 per share. As of December 31, 2014, we have no available credit under the SVB Loan.

In December 2011, in conjunction with our facility lease, we issued a $2.0 million subordinated convertible unsecured promissory note to the venture arm of our landlord, BioMed Realty, L.P., which was subsequently transferred to its affiliate, BMV Direct RE LP. The convertible note carries an annual interest rate of 8.0% and matures at the earlier of (i) May 2015, (ii) a liquidation event, or (iii) the closing of an initial firm commitment

underwritten public offering of our common stock pursuant to a registration statement under the Securities Act, unless previously converted. At any time prior to maturity, the holder may elect to convert the principal outstanding under the promissory note into shares of our Series D redeemable convertible preferred stock at the price of $2.662 per share. Upon conversion, all then accrued interest will be forgiven. As of December 31, 2014, the outstanding principal and accrued interest on the convertible note were $2.0 million and $0.5 million, respectively.

Cash Flows

The following table sets forth a summary of the net cash flow activity for each of the periods set forth below:

	Years Ended December 31,	
	2013	2014
	(in thousands)	
Net cash provided by (used in):		
Operating activities	$(17,311)	$(22,824)
Investing activities	(644)	(2,246)
Financing activities	50,737	2,512
Net increase (decrease) in cash	$ 32,782	$(22,558)

Operating activities. Net cash used in operating activities was $17.3 million and $22.8 million for the years ended December 31, 2013 and 2014, respectively. The net cash used in operating activities in each of these periods was primarily due to our net losses. The primary differences between net cash used in operating activities and our net loss in each period primarily related to non-cash charges for depreciation, stock-based compensation and changes in our prepaid and other assets, accounts payable and accrued expense accounts.

Investing activities. Net cash used in investing activities for the year ended December 31, 2013 was due to our purchases of property and equipment. Net cash used in investing activities for the year ended December 31, 2014 consisted of $0.2 million of property and equipment purchases and $2.0 million of net purchases of investments, consisting primarily of corporate debt and commercial paper.

Financing activities. Net cash provided by financing activities for the year ended December 31, 2013 was $50.7 million and consisted primarily of $38.7 million of net proceeds from the issuance of Series D redeemable convertible preferred stock, $9.5 million of net proceeds from the issuance of convertible notes that were converted into Series D redeemable convertible preferred stock and $2.5 million of net proceeds from the SVB Loan. Net cash provided by financing activities during the year ended December 31, 2014 consisted primarily of $5.0 million of proceeds from the SVB Loan offset by $1.6 million of principal payments on the SVB Loan and $1.0 million of costs paid in connection with our planned initial public offering.

Funding Requirements

We expect our expenses to increase in connection with our ongoing activities, particularly as we continue to advance Resolaris in clinical development, continue our research and development activities with respect to potential Physiocrine-based therapeutics, and seek marketing approval for Resolaris and other product candidates that we may develop. In addition, if we obtain marketing approval for any of our product candidates, we expect to incur significant commercialization expenses related to product sales, marketing, manufacturing and distribution. We currently have no sales or marketing capabilities and would need to expand our organization to support these activities. Furthermore, upon the completion of this offering, we expect to incur additional costs associated with operating as a public company. Accordingly, we will need to obtain substantial additional

funding in connection with our continuing operations. Our forecast of the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement that involves risks and uncertainties, and actual results could vary materially.

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

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

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

Contractual Obligations and Commitments

The following table summarizes our contractual obligations as of December 31, 2014:

		Payments Due by Period			
	Total	Less than 1 Year	1-3 Years	3-5 Years	More than 5 Years
		(in thousands)			
Commercial bank debt, including interest and final payment obligations	$ 9,554	$ 3,622	$5,932	$ —	$ —
Convertible promissory note, including interest	2,544	2,544	—	—	—
Operating lease obligation (1)	1,431	590	841	—	—
Total	$13,529	$ 6,756	$6,773	$ —	$ —

(1) Our operating lease obligations relate to our corporate headquarters in San Diego, California. We lease 17,083 square feet of office and laboratory space under an operating lease that expires in May 2017.

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 for operating purposes. These contracts generally provide for termination after a notice period, and therefore are cancelable contracts and not included in the table of contractual obligations and commitments.

We may have payment obligations under our agreements with The Scripps Research Institute, or TSRI, certain of which are contingent upon future events such as our achievement of specified development, regulatory and commercial milestones, and we are required to make development milestone payments and royalty payments in connection with the sale of products developed under these agreements. As of December 31, 2014, we were unable to estimate the timing or likelihood of achieving the milestones or making future product sales and, therefore, any related payments are not included in the table above.

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

Recent Accounting Pronouncements

In June 2014, the Financial Accounting Standards Board, or FASB, issued Accounting Standards Update, or ASU, No. 2014-10, *Development Stage Entities (Topic 915) Elimination of Certain Financial Reporting Requirements, Including an Amendment to Variable Interest Entities Guidance in Topic 810, Consolidation*. This ASU, among other things: (i) eliminates the requirement to present inception-to-date information on the statements of income, cash flows, and stockholders' equity, (ii) eliminates the need to label the financial statements as those of a development stage entity, (iii) eliminates the need to disclose a description of the development stage activities in which the entity is engaged and (iv) amends FASB ASC 275, *Risks and Uncertainties*, to clarify that information on risks and uncertainties for entities that have not commenced planned principal operations is required. The amendments in ASU No. 2014-10 related to the elimination of Topic 915 disclosures and the additional disclosure for Topic 275 are effective for public companies for annual and interim reporting periods beginning after December 15, 2014. We have early adopted this new guidance for our consolidated financial statements for the year ended December 31, 2013, and therefore have not labeled our consolidated financial statements as those of a development stage entity or included the previously required inception-to-date information.

In August 2014, the FASB issued ASU 2014-15, *Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern*. ASU 2014-15 requires management to evaluate relevant conditions, events and certain management plans that are known or reasonably knowable that when, considered in the aggregate, raise substantial doubt about the entity's ability to continue as a going concern within one year after the date that the financial statements are issued, for both annual and interim periods. ASU 2014-15 also requires certain disclosures around management's plans and evaluation, as well as the plans, if any, that are intended to mitigate those conditions or events that will alleviate the substantial doubt. ASU 2014-15 is effective for fiscal years ending after December 15, 2016. We are currently evaluating the impact that the adoption of ASU 2014-15 will have on our consolidated financial statements and related disclosures.

Off-Balance Sheet Arrangements

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

Quantitative and Qualitative Disclosures about Market Risk

Interest Rate Risk

Our primary exposure to market risk is interest income sensitivity, which is affected by changes in the general level of U.S. interest rates. Due to the short-term duration of our investment portfolio and the low-risk profile of our investments, we would not expect our operating results or cash flows to be affected to any significant degree by the effect of a sudden change in market interest rates on our investment portfolio. A 10% change in interest rates on December 31, 2014 would not have had a material effect on the fair market value of our portfolio.

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

Our debt obligations bear interest at fixed rates and therefore have no exposure to changes in interest rates.

Foreign Currency Exchange Risk

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

Effects of Inflation

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

BUSINESS

Overview

We engage in the discovery and clinical development of innovative medicines for patients suffering from severe, rare diseases using our knowledge of Physiocrine biology, a newly discovered set of physiological modulators. We have discovered approximately 300 Physiocrines (*physio* for life and *crine* for specific activity), a class of naturally occurring proteins that we believe promote homeostasis, a fundamental process of restoring stressed or diseased tissue to a healthier state. Physiocrines are extracellular signaling regions of tRNA synthetases, an ancient family of enzymes that catalyze a key step in protein synthesis. We believe that Physiocrines have evolved over time to modulate important cellular pathways by interacting with various types of cells, including immune and stem cells. Approximately 100 of these proteins interact with the immune system, which we believe presents a significant therapeutic opportunity to restore affected tissues to a healthier state through natural immuno-modulation mechanisms. We successfully completed a Phase 1 clinical trial of Resolaris, our first development candidate from our discovery engine, and are currently conducting a multi-national exploratory Phase 1b/2 clinical trial of Resolaris in adult patients with facioscapulohumeral muscular dystrophy, or FSHD, a severe, rare genetic myopathy with an immune component, for which there are currently no approved treatments. By leveraging our discovery engine and our knowledge of rare diseases, we aim to build a proprietary pipeline of novel product candidates with the potential to treat severe, rare diseases characterized by immune dysregulation. We plan to independently commercialize our Physiocrine-based therapeutics.

Our scientists were the first to identify the Resokine pathway (*reso* for restoring skeletal muscle health and *kine* for activity related to cytokines), an extracellular pathway in human skeletal muscle tissue associated with activities arising from various Physiocrine regions of the histidine aminoacyl tRNA synthetase, or HARS. We believe that the Resokine pathway, among its various activities, modulates the immune system to promote tissue homeostasis. We believe the Resokine pathway may play an important role in muscle and lung health. Certain patients with antisynthetase syndrome, a rare auto-immune disease, have antibodies to HARS, which are known as Jo-1 antibodies. These Jo-1 antibody patients often develop two significant clinical manifestations, skeletal inflammatory myopathy and interstitial lung disease, or ILD. We believe that the binding of Jo-1 antibodies, particularly to the immuno-modulatory domain of HARS, or iMod domain, blocks HARS immuno-modulatory functions and results in the muscle and lung disease in these Jo-1 antibody patients.

We are harnessing the Resokine pathway and its association in skeletal muscle with homeostasis to develop Resolaris as a first-in-class therapeutic for patients with severe, rare myopathies with an immune component, or RMICs, for which there are limited or no approved treatments. A myopathy is a disease of skeletal muscle tissue, characterized by muscle fiber deterioration, muscle weakness and often an immune response in the affected muscle tissue. In contrast to most current immunology drugs, which are engineered antagonists of immunological pathways, Resolaris is derived from a naturally occurring protein, HARS, which we believe has the potential to reset the immune system in diseased tissue to a more normal state while maintaining the immune system's activity against exogenous, pathogen-based insults. We observed that stimulation of the Resokine pathway through the introduction of Resolaris and its derivatives in rodent models of both severe inflammation and myopathy led to immuno-modulatory effects. We have shown that stimulation of the Resokine pathway by Resolaris alters immune responses and the expression or release of immune-related proteins from cells in response to inflammation. HARS, which contains the immuno-modulatory domain, is also released from human skeletal muscle. In addition to its immuno-modulatory properties, we believe the Resokine pathway may act on other physiological processes, including processes associated with stem cells, fibrosis and endothelial cells.

Since the identification of the Resokine pathway, we have successfully advanced Resolaris through preclinical development, current Good Manufacturing Practice, or cGMP, manufacturing and an initial Phase 1 clinical trial. In the first quarter of 2014, we completed a double-blind, placebo-controlled Phase 1 clinical trial of Resolaris, in which we assessed its safety and tolerability in 32 healthy subjects. Resolaris was shown to be well tolerated at all doses tested, and no serious adverse events were reported. Based on the favorable clinical safety, pharmacokinetic and immunogenicity profile of Resolaris in this trial, we decided to advance Resolaris into clinical trials of RMIC patients.

We are currently conducting a multi-national exploratory Phase 1b/2 clinical trial of Resolaris in adult patients with FSHD in the European Union. This randomized, double-blind, placebo-controlled trial is designed to evaluate the safety, tolerability, pharmacokinetics and immunogenicity of multiple intravenous doses of Resolaris in adults with FSHD. We also intend to explore pharmacodynamic changes in inflammatory immune responses in skeletal muscle, as assessed by quantitative magnetic resonance imaging, or MRI, and in peripheral blood, as assessed by levels of circulating immune proteins, such as cytokines and muscle enzymes, and *ex vivo* inflammatory immune proteins released from peripheral blood cells. Resolaris will be studied in three dose escalation cohorts (0.3 mg/kg, 1.0 mg/kg and 3.0 mg/kg). In the fourth quarter of 2014, we completed multiple dosing of the patients in the first dose cohort. We recently completed dosing patients in the second cohort and, in April 2015, our independent Data Monitoring Board, or DMB, for the trial recommended that we proceed with the third cohort. We are currently enrolling patients in the third cohort. Subject to our interactions with regulatory authorities and patient enrollment in accordance with our clinical development plans, we expect to report initial results from this clinical trial in the fourth quarter of 2015 or early 2016.

Our initial therapeutic efforts target severe, rare disease indications in which patients suffer from the immune-related consequences of their genetic disease. We have identified over 20 distinct, molecularly definable RMIC indications, including FSHD and limb-girdle muscular dystrophies, or LGMD, in which we believe Resolaris has the potential to target the immune component of these genetic diseases.

We are also harnessing the Resokine pathway and its potential role in lung disease, specifically ILD, to develop Resolaris as a therapeutic for patients with rare pulmonary diseases with an immune component, or RPICs. ILD is associated with Jo-1 antibody patients and occurs in multiple other clinical settings. We are currently evaluating these other forms of ILD to identify the most appropriate RPIC indication for the initial clinical assessment of augmenting the Resokine pathway with Resolaris.

We have initiated a discovery program to explore varying exposures of the iMod domain of the Resokine pathway through protein engineering. The program seeks to develop a potential therapeutic that we refer to as iMod.Fc. We also believe our proprietary inventory of Physiocrines and their diverse functions have potential therapeutic application in a variety of diseases characterized by tissue dysfunction, including severe diseases of the lung, gut, skin, brain and liver. We intend to leverage our unique understanding of Physiocrines and our broad intellectual property portfolio, which we believe covers this entire class of potential protein therapeutics, to build a pipeline of product candidates that we expect to develop and commercialize independently for the treatment of various rare diseases.

We were founded in 2005 by Paul Schimmel, Ph.D. and Xiang-Lei Yang, Ph.D., two leading aminoacyl tRNA synthetase scientists at The Scripps Research Institute in San Diego, California. Our Executive Chairman and Chief Executive Officer, John D. Mendlein, Ph.D., was formerly the Chief Executive Officer of Adnexus Therapeutics, Inc. (acquired by Bristol-Myers Squibb Company) and Affinium Pharmaceuticals, Ltd. (acquired by Debiopharm Group), and held various roles at Aurora Biosciences Corporation (acquired by Vertex Pharmaceuticals Incorporated). We have assembled an executive team with broad experience in the discovery, development and commercialization of innovative therapeutics, including transformative therapies for rare genetic diseases such as Kalydeco, marketed by Vertex Pharmaceuticals Incorporated for the treatment of cystic fibrosis. We are advised by a Therapeutic Advisory Board and a Scientific Advisory Board, both comprised of leaders in the field of biology for medical applications, including our special advisor in immunology, Bruce Beutler, M.D., recipient of the 2011 Nobel Prize in Physiology or Medicine for his work in immunology. Our key investors include entities affiliated with Alta Partners; Cardinal Partners; Domain Associates; Fidelity Management & Research Company; Polaris Partners and Sofinnova Ventures.

Our Strategy

We aim to capitalize on Physiocrine biology, a new and important area of human biology, to develop first-in-class medicines to treat patients with severe diseases characterized by an immune component. Key elements of our strategy include the following:

- ***Leverage our leadership position in Physiocrine biology to develop and commercialize novel, first-in-class medicines for patients affected by severe, rare diseases with significant unmet need.*** We focus on patients with severe, rare genetic diseases because we believe that the stimulation of Physiocrine pathways in these patients can restore diseased tissue to a more normal phenotype. Our strategy is to focus initially on indications where current treatment options are limited and our product candidates have the potential to provide transformative therapeutic benefit to patients given the severity of the diseases. We believe our initial focus on rare diseases will allow us to more effectively deploy investor capital for the independent development and commercialization of medicines for the benefit of patients and our stakeholders.
- ***Rapidly and prudently pursue the development and commercialization of Resolaris to treat patients across multiple severe disease indications.*** We intend to expeditiously pursue the development and regulatory approval of Resolaris in multiple RMICs. We are currently evaluating Resolaris in a Phase 1b/2 clinical trial in adult patients with FSHD and expect to report initial results from this clinical trial in the fourth quarter of 2015 or early 2016. In addition, we plan to initiate clinical trials in early onset FSHD and other RMIC indications, including limb-girdle muscular dystrophy. We also intend to evaluate Resolaris in other rare diseases with an immune component, such as RPIC indications. To bolster our clinical understanding of Resolaris, we may additionally evaluate Resolaris in more common diseases with an immune component.
- ***Leverage our discovery engine to build a pipeline of first-in-class Physiocrine medicines to address severe conditions characterized by immune pathway dysfunction or fibrosis.*** Based on our understanding of the biology of Physiocrines, we believe that this class of naturally occurring proteins has the potential to produce therapeutic benefits across a broad range of disease indications associated with an inappropriately amplified immune response, or where fibrosis contributes to disease associated with specific organs. We plan to leverage our discovery engine to identify other Physiocrine pathways of interest and select additional potential product candidates for preclinical and clinical investigation in a variety of disease settings on a tissue-by-tissue basis, which may include severe, currently inadequately treated diseases of the lung and liver.
- ***Retain exclusive worldwide commercial rights to our product candidates to pursue autonomous commercialization.*** We intend to build a pipeline of product candidates, the rights to which we solely own or exclusively license, that we can commercialize independently through a relatively small, dedicated commercial organization focused on patient needs and directed at a limited number of physicians who specialize in the treatment of our target patient populations. While we do not expect to require pharmaceutical partners for commercialization of our product candidates, we may consider partnering for strategic purposes, including to enhance our pipeline efforts.
- ***Expand our knowledge and intellectual property position in Physiocrine biology by emphasizing continuous scientific and business improvements.*** We will continue to aggressively pursue new scientific and therapeutic insights into Physiocrine biology through internally developed *in vivo* and *in vitro* screening systems in conjunction with genetic analysis and disease associations of Physiocrines, as well as in partnership with academic institutions and disease societies. We intend to leverage our leadership position in this field to broaden our intellectual property positions both in our most advanced programs and for additional therapeutic applications of Physiocrines. We will continue to vigorously prosecute and defend our patent portfolio, as well as exploit our proprietary position to strategically advance our business.
- ***Build a world class organization oriented to patients and focused on rigorous scientific, clinical and industrial advancements.*** We have assembled a world class team with industry-recognized expertise in biology, medicine and the commercialization of innovative and important therapeutics. We intend to

continue to build on our leadership position in Physiocrine and immunology-based therapeutics and to grow an organization and culture dedicated to the development and commercialization of medicines with the potential to positively transform the lives of patients with severe, rare diseases. We intend to maintain and expand our relationships with key opinion leaders, patient advocacy groups and other business partners, and to solicit input from payors and others in the healthcare industry, to identify and develop our product opportunities and to design our development programs in order to maximize the availability of our product candidates to patients.

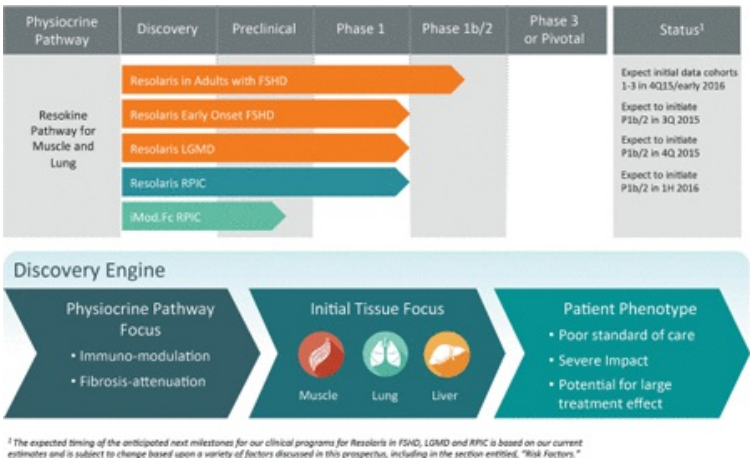
Our Founding Principles

We embrace the following principles:

- We understand disease never takes a day off. Transformational science never sleeps in order to make meaningful medicines.
- With relentless determination, we aim to discover life-changing therapies for people with grave maladies where others fall short.
- We aim to develop medicines by orchestrating important physiological processes using novel biological and therapeutic mechanisms.
- We recruit and retain remarkable people to actualize our aspiration to achieve industry-admired results in all aspects of our business.
- We galvanize our teams using shared principles to accomplish our collective mission to make meaningful medicines with the potential to provide positive outcomes to patients and our stakeholders.

Our Pipeline—A New Set of Treatment Mechanisms for Patients

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



[1] The expected timing of the anticipated next milestones for our clinical programs for Resolaris in FSHD, LGMD and RPIC is based on our current estimates and is subject to change based upon a variety of factors discussed in this prospectus, including in the section entitled, "Risk Factors."

Our research suggests that Physiocrines act through basic mechanisms of innate and adaptive immunity, as well as other pathways, in a way that is distinct from existing classes of protein therapeutics. We believe Physiocrines have evolved, among other things, to balance the immune system, resolving inflammation naturally, in contrast to currently available immuno-modulatory therapeutics, which are engineered inhibitors of pro-inflammatory pathways. We intend to harness these mechanisms of Physiocrines to benefit patients with severe diseases in ways that we believe have advantages over traditional antibody and small molecule approaches.

Physiocrines: Harnessing a Newly Discovered Source of Innovative Therapeutics

The Promise of Physiocrine-Based Medicines in Promoting Homeostasis

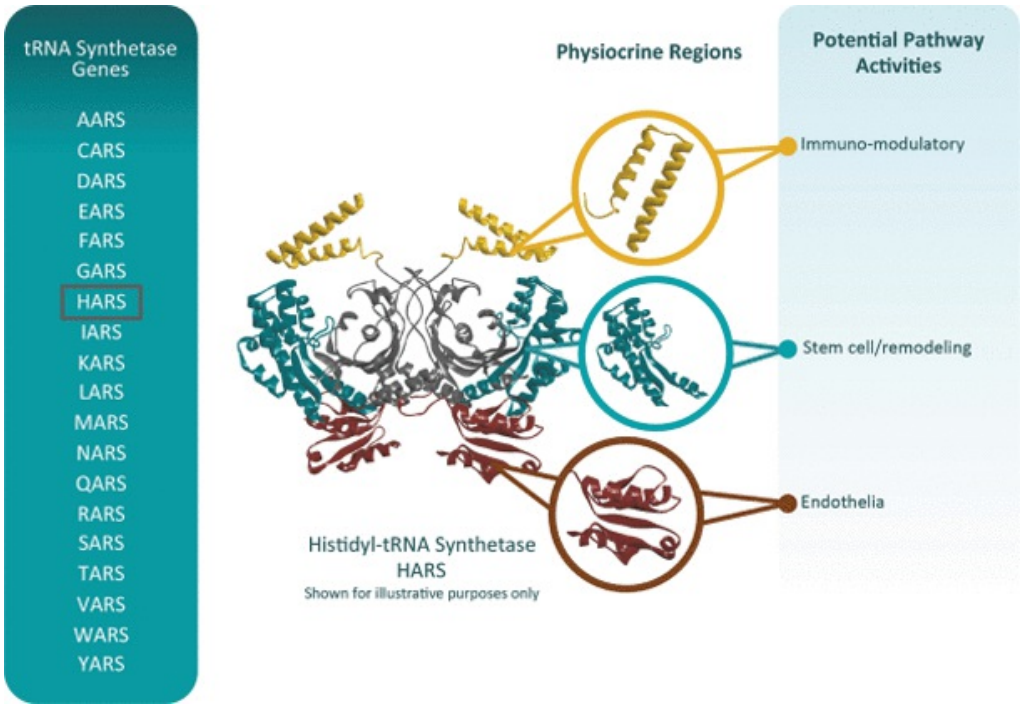
Homeostasis, or the coordinated regulation of tissues within the body, is fundamental to the maintenance of the overall health of an organism and a key feature of multicellular life. Lack of homeostasis can lead to disease and death. The process of homeostasis was first described in 1865 by the French physiologist Claude Bernard and Walter Cannon later coined the term. In the 150 years since this discovery, many proteins associated with homeostatic pathways have been discovered, ranging from insulin to erythropoietin, or EPO.

Using our knowledge of bioinformatics, sequencing, proteomics and structural biology, we identified Physiocrines, a novel class of proteins that are present as biologically active signaling regions of the tRNA synthetases, an ancient protein family. We believe that Physiocrines are involved in orchestrating homeostatic activities to help the body restore diseased or damaged tissue to a healthier state. We have observed that certain Physiocrines exhibit previously undescribed extracellular activities that are involved in restoring and regulating tissues to promote health. We believe that physiological perturbations, such as stress or changes in physiological state, alter or induce the release of Physiocrines from cells or platelets in the human body. Physiocrines have been observed to be released from a wide variety of cells, including in response to such stimuli as starvation-induced apoptotic stress or the introduction of certain cellular ligands, including tumor necrosis factor alpha and vascular endothelial growth factor.

Physiocrine Biology Overview

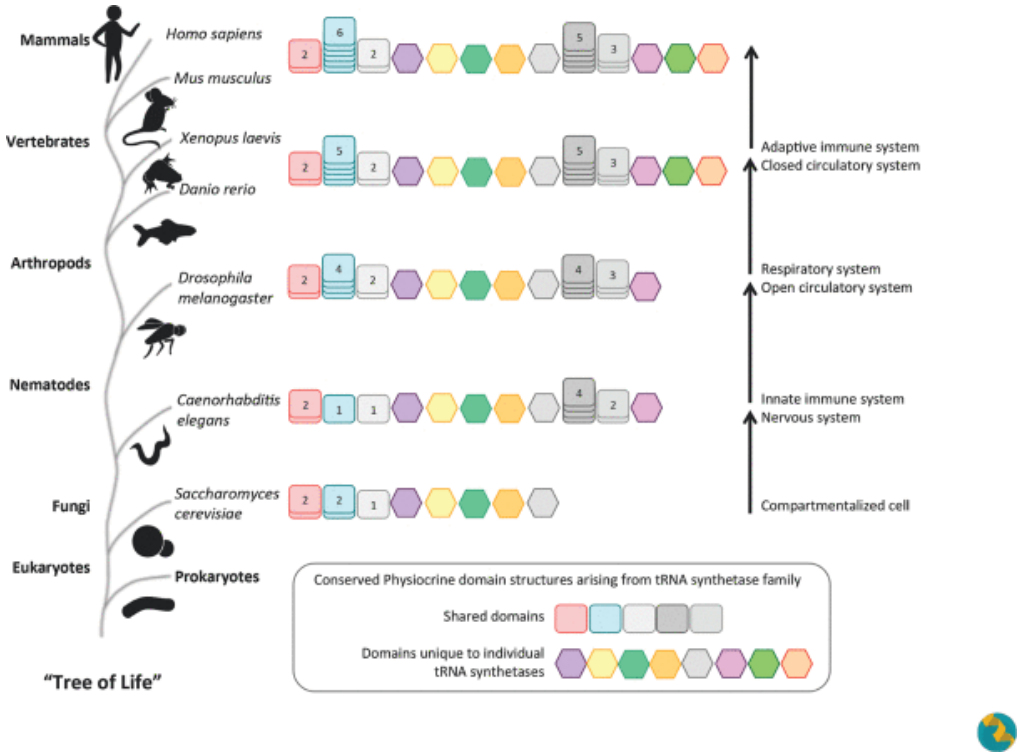
The Discovery of Physiocrines

In 1999, our founder, Dr. Paul Schimmel, published in *Science* a structural and functional description of extracellular signaling regions of a specific aminoacyl tRNA synthetase. tRNA synthetases are an ancient family of enzymes that were generally thought to only be involved in protein synthesis. Since Dr. Schimmel's discovery, numerous papers have been published on the alternative activities of tRNA synthetases. We refer to the extracellular signaling regions of tRNA synthetases illustrated in the figure below, along with other later-discovered or splice variant regions of tRNA synthetases, as Physiocrines. A splice variant is a variation of a gene transcript.



There are 20 known human cytosolic tRNA synthetases, each coding for one of the 20 amino acids. Amino acids, when bonded together, form full-length functional proteins. There are about 15 potential Physiocrines on average per tRNA synthetase, including Physiocrine regions in a full length tRNA synthetase protein, splice variants from a tRNA synthetase gene, or proteolytic fragments from a full length protein. We believe Physiocrines interact with various proteins important in extracellular activities, including G protein-coupled receptors, cytokine receptors, tyrosine kinase receptors and extracellular matrix proteins.

Our founding mandate was to focus on the systematic interrogation of the tRNA synthetase gene family through bioinformatics and structural analysis. Our research, along with that of The Scripps Research Institute, revealed that although the genetic sequence of each of the 20 tRNA synthetase genes changed at multiple times over four billion years by the genetic mutation of tRNA synthetases, including the insertion of DNA sequences, protein synthesis, however, as characterized by tRNA synthetase activity, remained relatively unchanged over that period of time. As illustrated in the figure below, the structural diversity of proteins resulting from the inserted genetic material increased as living organisms became more complex and as fundamental physiological systems, including immunological, stem cell, muscular, circulatory, respiratory and neural systems, developed.



The results of this research suggested to us that tRNA synthetases retained a core function in protein synthesis over four billion years, while developing other important and diverse physiological functions associated with Physiocrines. We believe these functions could serve as a source of therapeutics directed at stimulating pathways involved in the restoration of homeostasis.

The Function of Physiocrines in Fundamental Pathways of Life

Based on the research suggesting that Physiocrines are potentially important modulators of cellular pathways, we hypothesized that Physiocrines may play roles in such fundamental processes as immunology, stem cell biology, neurology, vascular biology, skeletal muscle biology, hepatic (liver) biology and metabolic biology. To test this, we expressed and purified over 200 Physiocrine regions across the family of 20 tRNA synthetase genes and evaluated these purified Physiocrines in numerous cell-based assays to determine their activity in several important human physiological pathways. Some of the data were published in July 2014 in *Science*, with the data categorized according to important areas of biology. The table below describes several key areas of biology in which Physiocrines may present therapeutic opportunities:

Cellular Pathways	Number of Physiocrines	Potential Therapeutic Applications
Immunology	99	Rare Diseases with an Immune Component, Auto-immune Disorders, Oncology and Fibrosis
Stem Cells	129	Regenerative Medicine, Fibrosis and Oncology
Neurology	34	Neurodegenerative Diseases
Vascular	35	Cardiovascular Diseases, Oncology and Immunology
Skeletal Muscle	130	Skeletal Muscle Diseases
Hepatic	76	Liver Fibrosis
Metabolic	22	Diabetes and Obesity

Our current research includes efforts to understand the relationship of various Physiocrine pathways to health and disease and the potential for a particular Physiocrine pathway to provide a valuable therapeutic intervention point. In addition, various independent research sites across the world are conducting genetic analysis of DNA from patients with rare phenotypes and mutations to tRNA synthetases. Laboratories are also investigating the connection between tRNA synthetases and various cancers and auto-immune diseases.

Physiocrine Pathways as Therapeutic Intervention Points

Our Initial Focus on Immuno-Modulation

Many important therapeutics act in connection with physiological pathways, including growth factor and differentiation pathway agonists, such as insulin and erythropoietin, or EPO; growth factor pathway antagonists, such as vascular endothelial growth factor antagonists; immune pathway antagonists, such as tumor necrosis factor antagonists; immune pathway agonists, such as interferon; and metabolic pathway modulators, such as glucagon-like peptide-1 (GLP-1). We are initially focused on the application of Physiocrines to immuno-modulation in rare diseases. We selected immuno-modulation as our initial area of focus for the following reasons:

- We believe immunology plays a significant role in most diseases, including genetic diseases;
- A number of Physiocrines have been shown to be differentially expressed in immune cells;
- A large number of Physiocrine pathways appear to relate to immunology, as at least seven different tRNA synthetase proteins are associated with certain immune-driven diseases; and
- Approximately 100 Physiocrines have demonstrated activity in various cell-based assays related to immunological pathways.

Additionally, we focus our immuno-modulator development efforts on indications that represent severe, rare diseases, particularly genetically based diseases, because:

- Our scientific understanding of Physiocrines as immuno-modulators intersected with multiple rare diseases;
- We believe patients with rare genetic diseases often face challenges related to the responses of their immune systems to changes in tissues that are caused by their genetic mutations; and

- We believe the pathological immuno-phenotypes in rare diseases present an opportunity for us to therapeutically intervene with greater impact.

Advantages of Physiocrine-Based Therapeutics

Most current immunological drugs are engineered antagonists of immunological pathways, typically acting to lower elevated immune responses resulting from disease, as in the case of monoclonal antibodies acting against circulating signaling molecules, such as cytokines. Although these signaling molecules may be up-regulated in disease, their natural levels and fluctuations have evolved to include non-disease functions of the immune system, mediating a wide range of physiological activities, as opposed to evolving to cause or contribute to disease. Our discovery and development efforts focus on therapeutics derived from naturally occurring proteins. We believe that Physiocrines have naturally evolved to reset the immune system to control or reduce tissue damage while maintaining the immune system's activity against exogenous pathogen based insults, and may possess the following advantages over engineered antagonists of immunological pathways:

- As proteins designed by nature to reset the immune system, Physiocrines may provide a unique mechanism to improve patient outcomes through their activity in either a single or multiple pathways;
- Physiocrines have the potential to reset the immune system across multiple pathways at the level of an immune cell, rather than lowering the levels of a single immune protein like most engineered antagonists;
- Physiocrines may potentially act as agonists at the level of the immune cell to reduce pro-inflammatory effects and induce resolution of immune activity or inflammation;
- The therapeutic effects of Physiocrines may persist even after the Physiocrines have been cleared from circulation; and
- Physiocrines present the potential for fewer, if any, immuno-suppressive effects, as compared to engineered antagonistic immuno-modulators.

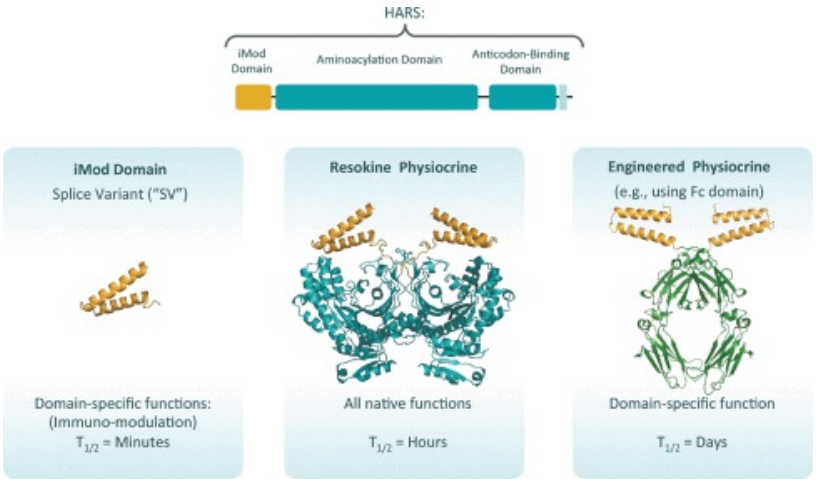
The Resokine Pathway and Resolaris, Our First Clinical Product Candidate

Identification of the Resokine Pathway through In Vivo Screening Approaches

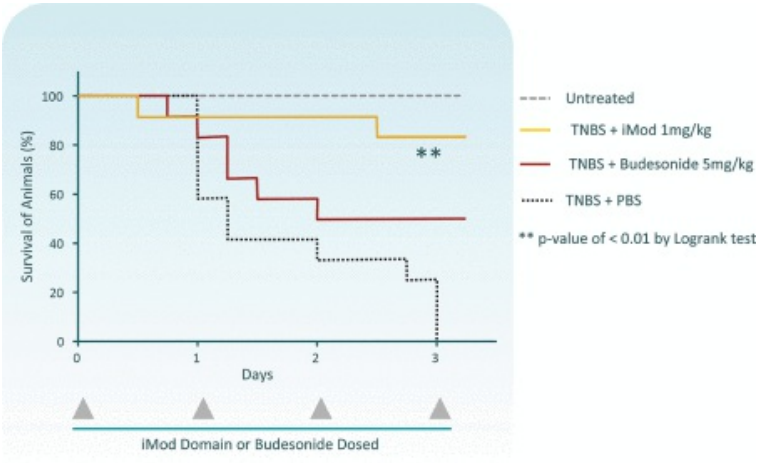
Our scientists discovered the Resokine pathway in human skeletal muscle using our *in vivo* screening systems in models of severe inflammation, combined with our knowledge of the effects of antibody binding to a specific tRNA synthetase in a population of patients with a particular rare myopathy. The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

First Demonstration of a Region of HARS as an Immuno-modulator

We conducted *in vivo* screening activities of a splice variant from HARS that we identified in our deep sequencing studies, which we refer to as the immuno-modulatory domain, or iMod domain, of HARS. The figure below depicts the iMod domain and other forms of HARS:



For our studies of the iMod domain, we selected a rodent model of severe immune cell activity or inflammation induced by the administration of trinitrobenzene sulfonic acid, or TNBS, in which the inflammation is thought to be driven by excessive T-cell involvement in the gut, leading to the death of the study animals. Animals administered the iMod domain survived longer than those given either the vehicle control phosphate buffer solution, or PBS, or an approved drug control (Budesonide) ($p<0.01$), demonstrating the potential activity of the iMod domain as an immuno-modulator of excessive T-cell involvement. The results of this study are summarized in the graph below:

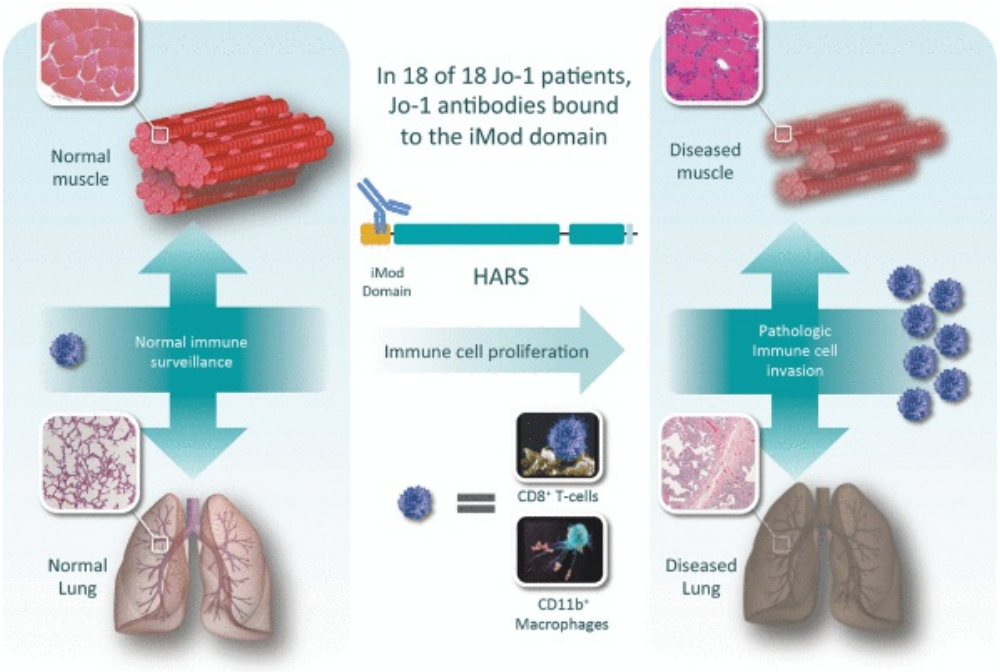


Additionally, we have demonstrated in the same rodent model of inflammation in the gut that at least two other related molecules, Resolaris and iMod.Fc, both of which are derived from HARS and contain the iMod domain, are active in models of excessive T-cell involvement. Based on these observations, we believe that blockade of the activity of the iMod domain may contribute to excessive or inappropriate T-cell involvement in immune-driven diseases.

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

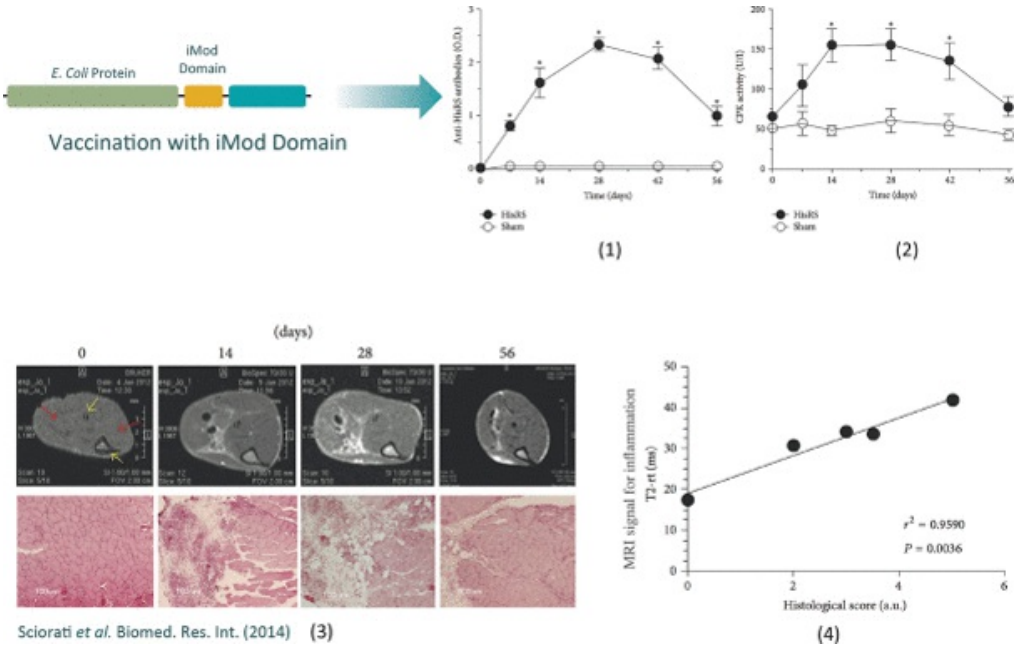
In 1983, Matthews and Bernstein published in *Nature* the observation that patients with a rare myopathy possessed antibodies to a single tRNA synthetase, HARS. Since then, it has been observed that patients with auto-antibodies to HARS (but not antibodies to the other 19 tRNA synthetases in the same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

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



Additional Confirmatory Studies of the Blockade of the Resokine Pathway in Animals

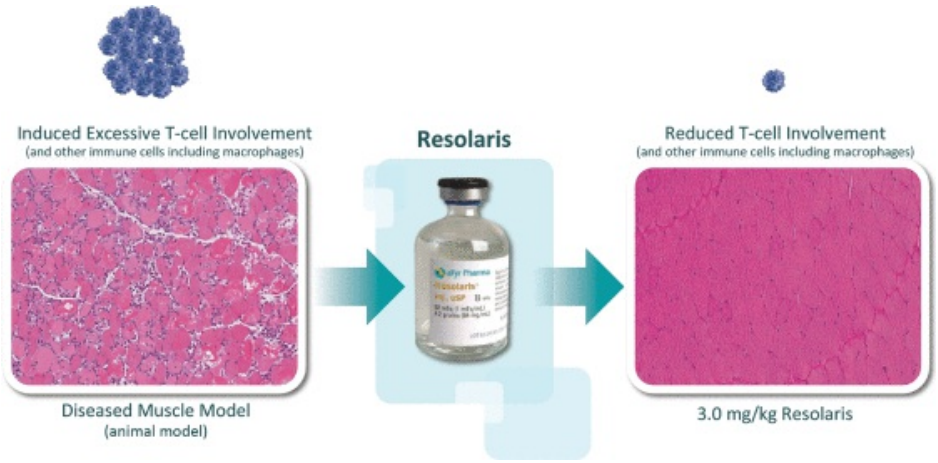
We have conducted studies that suggest that antibody blockade of the Resokine pathway contributes to immune cell invasion in skeletal muscle and lung tissue. Recently published animal studies by a third party laboratory are consistent with our findings. In particular, in 2014, Sciorati *et al*. published on the effect in rat skeletal muscle of antibodies to the iMod domain produced by vaccination, generating additional evidence that the Resokine pathway plays a role in skeletal muscle health and the immune system. The Sciorati study demonstrated: (1) antibody generation to the iMod domain of HARS; (2) levels of creatine kinase, or CK, a biomarker of muscle destruction, increased in relation to antibody levels; (3) antibodies to the iMod domain correlated with an increase in muscle inflammation, as observed by magnetic resonance imaging, or MRI; and (4) the MRI signal corresponded to muscle destruction, as judged by histology. These data are illustrated in the figures below:



The data generated by Sciorati *et al*. are consistent with our conclusions that the Resokine pathway was reduced or blocked in Jo-1 antibody patients as a result of antibodies against the iMod domain.

Altering Excessive T-cell Invasion in Preclinical Studies of Resolaris in Skeletal Muscle

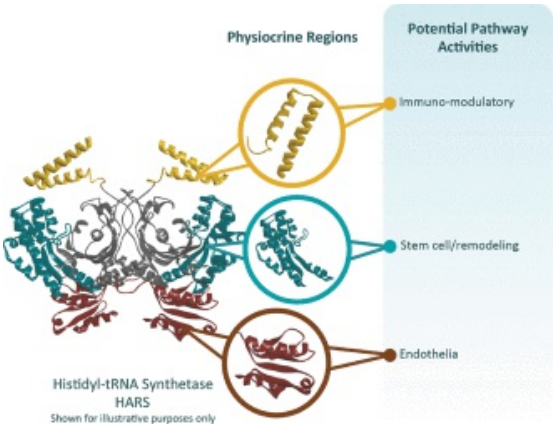
We also tested Resolaris in a rodent model in which statins, which are known to induce myopathies in humans and rodents, were administered to induce a severe, aggressive myopathy. In the study, rats were administered statins for two weeks, and at Day 8, treatment with Resolaris was started. After a week of daily treatment with Resolaris, we observed a dose dependent change in the histologic phenotype of the treated animals, from excessive immune cell invasion to nearly normal histology and immune cell levels, as compared to animals in the control group, as shown in the figure below:



Resolaris Mechanism of Action: T-cell Modulation and Other Potential Pathways

Our *in vivo* studies suggest that stimulation of the Resokine pathway through or with Resolaris combats pathophysiological changes in three established animal models of excessive T-cell involvement in which approved drugs have been tested. Our *in vitro* studies of Resolaris suggest that at least one of the activities of Resolaris includes a direct action on T-cells to reduce, but not completely block, cytokine release. This reduction also lasts for at least 24 hours after Resolaris has been removed from the T-cells. This suggests that the pharmacodynamic effect of Resolaris *in vivo* could be longer than the pharmacokinetics of the protein. It also suggests that there is at least one T-cell associated receptor for Resolaris, such as a cytokine or chemokine receptor. We observed Resolaris' effect on human T-cells by monitoring IL-2 levels over time.

Additional cell-based assays show that specific regions of Resolaris may harbor additional activities similar to Physiocrine regions from the HARS protein, including those illustrated in the figure below. We are currently conducting additional studies regarding non-immuno-modulatory activities that may relate to the mechanism of action of Resolaris.



Additionally, we have looked for direct antagonist activities of Resolaris on certain cytokines. Resolaris does not appear to act as a direct ligand antagonist, but rather appears to act more globally at the level of immune cells and potentially other cell types. HARS is also released directly from human skeletal muscle *in vitro*, and blocking HARS with antibodies after stimulated release by insulin-like growth factor, or IGF-1, reduces the effect of IGF-1 in muscle differentiation.

Resolaris for the Treatment of Multiple Rare Myopathies with an Immune Component (RMICs)

Overview

We are developing Resolaris as a first-in-class intravenous protein therapeutic for the treatment of rare myopathies with an immune component, or RMICs. We have identified over 20 distinct, molecularly definable RMIC indications that we believe Resolaris has the potential to treat. In each of these indications, skeletal muscle tissue exhibits dysfunction and becomes subject to immune cell invasion, which contributes to the loss of function and deterioration of the muscle tissue. RMIC patients generally present with three common characteristics:

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

In normal muscle, muscle mass and function require a balance between muscle cell stress and damage and muscle cell regeneration and growth. The immune system helps maintain this balance by “cleaning up” damaged muscle cells after muscle damage and during the healing process. In RMIC diseases, the balance is tipped to favor chronic pathophysiological muscle deterioration and persistent immune cell invasion. In genetically based RMIC diseases, aberrant protein expression often occurs, as in the case of FSHD patients with inappropriate expression of a protein not normally expressed in muscle. As discussed above, *in vivo* rodent models of skeletal muscle deterioration and immune cell invasion have shown that Resolaris can combat immune cell invasion into the muscle and muscle deterioration. Conversely, experiments in rodents have shown that antibody blockade of the Resokine pathway can lead to immune cell invasion and muscle tissue deterioration.

We intend to harness the body’s power to restore skeletal muscle after stress or damage in the development of Resolaris for RMIC patients who have limited or no approved treatment options. We believe Resolaris can offer a

potential multi-pharmacologic therapeutic, synergystically modulating multiple pathways important to muscle health. Our proprietary position for Resolaris includes an issued U.S. patent covering the composition of matter of Resolaris, as well as various patent applications relating to specific methods of use of Resolaris and related proteins.

Resolaris: Potential Specific Therapeutic Applications in RMICs

We believe Resolaris will provide therapeutic benefit to patients in RMIC indications characterized by excessive immune cell involvement, particularly a type of T-cell known as CD8 T-cells and macrophages. Dysregulated immune cell invasion can cause and exacerbate muscle damage and stress. For example, CD8 T-cells have been observed to contribute to muscle damage by the release of proteins that destroy or damage skeletal muscle cells. The table below describes RMIC indications in which the relationship between diseased muscle and the immune system has been observed by others, which we believe may be addressed by the proposed mechanism of action of Resolaris.

Disease Area	Type of RMIC	Molecular Definition of Disease (Estimated U.S. Population)	Immune Features	Potential Resolaris Mechanism of Action
Rare myopathies with an immune component (RMIC)	Genetic	Facioscapulohumoral muscular dystrophy, or FSHD (19,000) 3 genetic forms*	CD8 T-cell infiltration Macrophage infiltration Pro-inflammatory cytokine production, including: MCP-1, IL-6 and IL-12	In preclinical models *in vivo*, Resolaris reduces (i) the infiltration and accumulation of CD8 T-cells; (ii) the expression of cytokines, including MCP-1, IL-6 and others; and (iii) biomarkers, such as MMP9. *In vitro* studies using Resolaris also demonstrate reduction of a variety of pro-inflammatory cytokines, including IFN gamma and IL-17A, as well as the activity of pro-inflammatory macrophages.
		Limb-girdle muscular dystrophy, or LGMD (16,000) >20 genetic forms*	T-cell infiltration	
		Duchenne muscular dystrophy, or DMD (5,600-18,000) >50 genetic forms*	CD8 T-cell infiltration Macrophage infiltration MMP9, TIMP1, TNFα	
		>10 undisclosed muscular dystrophies	To be determined	
	Autoimmune	Sporadic Inclusion Body Myositis, or sIBM (3,400)	CD8 T-cell infiltration Macrophage infiltration Pro-inflammatory cytokine production, including MCP-1	
		Myositis with at least one molecular marker (such as auto-antibodies)		

* By use of the term "genetic form," we mean a molecularly defined marker that includes (1) changes in a chromosome structure, (2) different genes that are mutated or (3) a single gene with multiple points of mutation.

Legend:
IL-6: Interleutin-6
IL-12: Interleutin-12
MCP-1: Monocyte Chemotactic Protein 1
MMP9: Matrix Metallopeptidase 9
TIMP1: Tissue Inhibitor of Metalloproteinase-1
TNF-α: Tumor Necrosis Factor alpha

Resolaris: Our Clinical Development Program

We are discovering and developing protein based therapeutics leveraging the novel extra-cellular functions of tRNA synthetases to restore and maintain tissue homeostasis. The initial Physiocrine-based therapeutic from our discovery pipeline, Resolaris, has entered clinical development. We are pursuing a clinical development strategy that not only will inform the therapeutic potential of RMIC and RPIC indications but will also inform the therapeutic potential of Physiocrine-based therapeutics as a class. The strategy has as its foundation the extensive evaluation of the safety and tolerability of the administration of Physiocrine-based therapeutics to human subjects.

We successfully completed a single ascending dose Phase 1 clinical trial in healthy subjects of Resolaris, our first development candidate from our discovery engine for therapeutic applications of Physiocrines. We are currently conducting a multi-national Phase 1b/2 clinical trial of Resolaris in adult patients with facioscapulohumeral muscular dystrophy, or FSHD, a severe, rare genetic myopathy in which immune cells invade diseased skeletal muscle, for which there are currently no approved treatments.

We intend to initiate, in the third quarter of 2015, a clinical trial to assess the safety, tolerability, and biological and clinical activity of Resolaris in early onset FSHD patients. We intend to initiate, in the fourth quarter of 2015, a clinical trial to assess the safety, tolerability, and biological and clinical activity of Resolaris in a second RMIC population, LGMD patients. Finally, we intend to initiate, in the first half of 2016, a clinical trial to assess the safety, tolerability, and biological and clinical activity of Resolaris in an RPIC patient population.

Phase 1 Clinical Trial in Healthy Subjects

In the first quarter of 2014, we completed a single ascending dose Phase 1 clinical trial of Resolaris to assess its safety and tolerability in healthy subjects. The planning and design of the trial were guided by the principles that this trial would be the first time that a Physiocrine has been administered to a human subject, and that the therapeutic use of immuno-modulatory drugs are often characterized by poor tolerability and common safety concerns. In particular, we designed this trial as a double-blind, placebo-controlled study in order to rigorously assess safety and tolerability, such as injection site reactions or systemic reactions, and to assess the pharmacokinetics, or PK, immunogenicity and biological activity of single doses of Resolaris in humans. In this trial, 32 healthy adult subjects were randomized to receive a 30 minute intravenous infusion of either placebo or a single dose of 0.1 mg/kg, 0.3 mg/kg, 1.0 mg/kg, or 3.0 mg/kg of Resolaris. Participants were randomly assigned to receive Resolaris or placebo on a 3:1 basis so that within each of the four cohorts, six subjects received Resolaris and two subjects received placebo, and overall, 24 healthy subjects were dosed with Resolaris and eight healthy subjects were dosed with placebo.

Resolaris was found to be well tolerated in all dose cohorts in our Phase 1 clinical trial. There were no serious adverse events or deaths, and the incidence of individual treatment emergent adverse events, or TEAEs, among all groups was low, with no relationship to Resolaris dose level. All TEAEs observed in the trial were mild in intensity and transient, and resolved without treatment-related pathological effects. TEAEs that were considered possibly related to Resolaris were predominantly nervous system symptoms, including single cases of dizziness, headache, and drowsiness. No local tolerability issues related to Resolaris were observed.

We observed no significant changes from normal in over 30 cytokine and other immune-related protein assays after administration of 0.1 mg/kg, 0.3 mg/kg, 1.0 mg/kg, and 3.0 mg/kg of Resolaris in these healthy individuals. These results are consistent with the observed role of the Resokine pathway in resolving inflammation. Systemic exposure and C_{max} were dose proportional, mean total systemic clearance was low and the volume of distribution was small, resulting in a terminal half-life in plasma of approximately three to six hours across all dose levels. Low titer anti-drug antibodies were observed in five subjects out of 24 after administration of Resolaris. One subject out of 24 had similar low titer anti-drug antibodies prior to the administration of Resolaris. The PK of Resolaris was not altered in these subjects. Based on the favorable PK,
safety, tolerability and immunogenicity profile of Resolaris in our Phase 1 clinical trial in healthy subjects, we have advanced Resolaris into clinical development in RMIC patients.

Resolaris in Facioscapulohumoral Muscular Dystrophy (FSHD)

The process of selecting the first RMIC indication for our Resolaris program involved several steps. First, both genetic and autoimmune forms of RMIC were considered. Then, diseases with high unmet need (no treatment options), severe progressive disease manifestations and clear evidence of an immune component were selected for further exploration. Those in which the muscle tissue itself and the circulation clearly reflect the immune dysregulation were prioritized, with those whose immune pathogenesis overlapped with Resolaris activity rising to top of the list. These prioritized diseases included several distinct genetic myopathies.

Based on the indication selection process described above, we elected to first pursue FSHD, a rare genetic myopathy in which immune cells invade diseased skeletal muscle and for which there are no approved treatments. The primary clinical phenotype of FSHD is debilitating skeletal muscle deterioration and weakness. The symptoms of FSHD develop in an asymmetric pattern, starting with the face and upper body to the lower body and progressing in a “muscle by muscle” fashion. This is in contrast to other genetic myopathies such as Duchenne muscular dystrophy that usually affect groups of muscles concurrently and symmetrically. These symptoms include musculoskeletal abnormalities such as abnormal protrusion of the shoulder blades or exaggerated bend of the lower spine and, often as the disease progresses, difficulty standing upright, lifting objects, reaching above shoulder level or using the shoulders to support various activities of daily life. Patients also suffer pelvic girdle and lower limb weakness, resulting in progressive difficulty arising from a seated position. Importantly, most patients eventually develop profound weakness in the lower leg and cannot manage to lift the foot of the affected side appropriately. This condition results in frequent falls and related injuries. In addition to debilitating muscle weakness, FSHD patients often experience severe fatigue, muscle deterioration and pain. While FSHD can manifest at any age, the onset of symptoms in many patients occurs before the age of 18. We refer to this patient population as early onset FSHD. Within this early onset population are individuals with symptom onset at less than five years of age, with progression in disease prior to age ten. These individuals have the most severe muscle symptoms and significant extra-muscular manifestations such as auditory deficits and retinal complications that may result in vision loss. This sub-group of early onset patients are often referred to as having “infantile onset” FSHD.

While estimates of FSHD prevalence vary, studies exploring the topic have identified average prevalence rates of approximately one in 17,000. Applying this rate to the U.S. population, as of November 1, 2014, yields a domestic FSHD population of approximately 19,000. The disease is typically diagnosed by the presence of a characteristic pattern of muscle weakness and other clinical symptoms, as well as through genetic testing of the number of repeats of a specific DNA sequence at the end of Chromosome 4. In normal, unaffected individuals this chromosomal region has from 11 to 100 repeats of the applicable DNA sequence. Patients with late or adult onset FSHD typically have only one to ten of these repeats. The most severe form of FSHD is associated with three or fewer repeats. The term FSHD1 is used to delineate patients in which the genetic basis relates to the deletion of these repeats at the end of Chromosome 4. Another form of the disease, FSHD2, occurs in approximately 5% of FSHD patients, and is caused by mutations in the gene *SCHMD1* located on Chromosome 18 of the applicable DNA sequence. In both FSHD1 and FSHD2, the genetic abnormality results in the expression of genes that are normally silent or inactive in skeletal muscle. Consequently, an unusual profile of proteins is produced, which has been linked to FSHD skeletal muscle pathology.

The FSHD immuno-pathology includes an infiltrative inflammatory process (usually dominated by CD8 T-cells and macrophages) that can also be observed by MRI in individual skeletal muscles that are in the early stages of disease. Longitudinal MRI studies in FSHD have recently shown that these muscle by muscle inflammatory changes directly precede the fatty infiltration that characterizes individual muscles that have been affected for a longer period of time. Once this fatty infiltration has progressed to a certain stage in the affected muscle, however, the level of inflammation as detected by MRI decreases. The degree of fatty infiltration correlates with a commonly used measure of functional status, the FSHD clinical severity score.

The inflammatory immune response in FSHD is reflected in individuals with FSHD through activated immune cells and elevated levels of immune and skeletal muscle proteins present in the circulation. Peripheral blood mononuclear cells from individuals with evidence of muscle inflammation also show evidence of activation in cell culture by spontaneously releasing high amounts of immune proteins into the culture medium compared to controls.

There are currently no approved treatments for FSHD. The standard of care in management of the disease includes physical therapy and, in the presence of severe muscle weakness, orthotic devices or surgical interventions may be needed to maintain musculoskeletal stability.

Phase 1b/2 Clinical Trial

In the third quarter of 2014, we initiated a multi-national Phase 1b/2 clinical trial of Resolaris in adult patients with FSHD in the European Union. The randomized, double-blind, placebo-controlled trial is designed to evaluate the safety, tolerability, PK and immunogenicity of multiple intravenous doses of Resolaris in adults 18 to 65 years of age with FSHD. We also intend to explore pharmacodynamics, or PD, changes in inflammatory immune responses in skeletal muscle, as assessed by quantitative MRI, and in peripheral blood, as assessed by measures of circulating immune proteins such as cytokines and muscle enzymes and *ex vivo* inflammatory immune proteins released from peripheral blood cells. We initially received regulatory clearance to proceed with our trial at clinical sites in France, Italy and the Netherlands. These sites were selected based on their clinical expertise and their leadership and expertise in MRI as an assessment tool for FSHD patients. Additionally, in January 2015, we received clearance from the FDA to initiate our Phase 1b/2 clinical trial of Resolaris in adult patients with FSHD in the United States, subject to a partial clinical hold that prohibits the evaluation of Resolaris at doses higher than 3.0 mg/kg. We do not expect the partial clinical hold to have a material impact on the timeline for this clinical trial because we currently do not plan to evaluate Resolaris doses higher than 3.0 mg/kg in the United States.

Resolaris will be studied in three dose escalation cohorts (0.3 mg/kg, 1.0 mg/kg and 3.0 mg/kg). The DMB for the trial will meet to review the clinical data from each cohort, and will provide us with a recommendation regarding advancement into the next cohort. In each cohort, patients will be randomized to receive Resolaris or placebo at a ratio of 3:1. Patients in the first two cohorts will be dosed over a period of one month, and patients in the third cohort will be dosed over a period of three months. We enrolled a total of four patients in the first cohort and eight patients in the second cohort, and expect to enroll eight patients in the third cohort. In the fourth quarter of 2014, we completed multiple dosing of the patients in the first dose cohort. We recently completed dosing patients in the second cohort, and in April 2015, the DMB recommended that we proceed with the third cohort. We are currently enrolling patients in the third cohort. Starting with the second cohort, inclusion criteria included the presence of at least one skeletal muscle in the lower extremities displaying an inflammatory immune response by MRI. Our protocol for this trial includes the option to initiate up to two additional cohorts comprised of 12 patients each. We intend, either through study specific extensions or a dedicated clinical trial protocol, to evaluate the safety, tolerability and clinical activity of extended treatment of FSHD patients with Resolaris.

Subject to our interactions with regulatory authorities and patient enrollment in accordance with our clinical development plans and following our receipt of unblinded clinical safety, MRI and PD data from all three cohorts, we expect to report initial results from the trial in the fourth quarter of 2015 or early 2016.

In parallel with conducting our initial clinical trial in adults with FSHD, we are finalizing our plans to evaluate Resolaris in a multi-center, international trial of patients with early onset FSHD. This trial will be designed to assess the safety, tolerability, PK, immunogenicity, PD and clinical effectiveness of multiple intravenous doses of Resolaris in patients with early onset FSHD. Subject to our interactions with regulatory authorities, we expect to initiate this clinical trial in the third quarter of 2015.

In the first quarter of 2015, the European Commission granted orphan medicinal product designation for Resolaris (ATYR1940) for the treatment of FSHD following a positive opinion by the EMA's Committee of Orphan Medicinal Products. In the second quarter of 2015, the FDA granted orphan drug designation for Resolaris (ATYR1940) in the United States for the treatment of FSHD.

Resolaris in Other RMIC Indications

In addition to FSHD, we plan to address other genetic diseases in which immune cells invade diseased muscle. We plan to commence clinical trials of Resolaris in at least one form of limb-girdle muscular dystrophy, or LGMD, in adult patients in the fourth quarter of 2015.

LGMD is a broad term used to describe over 20 rare genetic myopathies. The mutations typically create abnormal, malfunctioning proteins. These diseases are linked by the common distribution of their muscle weakness (e.g., predominantly in the proximal limb muscles and the pelvic and shoulder girdle muscles). As is the case with FSHD patients, some LGMD patients typically suffer from:

- skeletal muscle weakness or compromised function in identifiable, specific muscles;
- skeletal muscle immune cell invasion in identifiable, specific muscles; and
- skeletal muscle deterioration in identifiable, specific muscles with insufficient muscle regeneration.

The LGMD disorders stem from deficits in proteins that are important for muscle integrity. In some forms, the affected muscles can be more fragile than normal muscle and are easily damaged, even in the setting of everyday stress. The associated immune cell invasion and muscle deterioration can be seen locally in muscle tissue by biopsy or imaging techniques, such as MRI. The muscle deterioration is also reflected systemically, with patients often displaying elevated levels of muscle proteins in their blood (e.g., CK) or urine (e.g., myoglobin).

The age of onset of certain forms of LGMD is usually between ten and 30, with both genders affected equally. The disease inevitably gets worse over time, although progression is more rapid in some patients. The disease commonly leads to dependence on a wheelchair within twenty to thirty years of symptom onset, but there is high inter-patient variability, with some patients maintaining mobility. LGMD may eventually weaken the respiratory muscles, leading to illness or early death due to complications from this secondary manifestation. Individuals with cardiac involvement may succumb to heart failure.

No definitive treatments exist for any of the over 20 forms of LGMD. Clinical management is directed to prolong survival and improve quality of life, including avoiding obesity, promoting physical therapy and stretching exercises, using mechanical aids to help ambulation and mobility, surgical intervention for orthopedic complications, using respiratory aids when indicated, monitoring for cardiomyopathy in LGMD types with cardiac involvement, and social and emotional support and stimulation.

We are in the process of evaluating the various genetic forms of LGMD in order to select genetic forms that we believe will be most amenable to treatment with Resolaris, based on factors such as the characteristics of the associated immuno-pathology in skeletal muscle. Subject to our selection of one or more genetic forms of LGMD for clinical evaluation, we may apply for orphan designation for Resolaris in an LGMD indication in one or more territories, which may include the United States and Europe.

Resolaris Non-Muscle Indication Set: Rare Pulmonary Diseases with an Immune Component (RPICs)

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

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

ILD occurs in other settings such as rare genetic disorders, environmental exposures, as a side effect of certain therapeutics and as a manifestation of certain connective tissue disorders. Among these forms of ILD, we have identified several that result in severe and progressive lung disease and share immune-pathophysiology features that overlap with our demonstrated Resolaris activities. We have classified these disorders as rare pulmonary diseases with an immune component, or RPIC. Examples of RPICs include idiopathic non-specific interstitial pneumonias, idiopathic pulmonary fibrosis, lymphocytic interstitial pneumonia, bleomycin (the chemotherapeutic agent)-induced pulmonary fibrosis, and ILD in the setting of systemic sclerosis, or scleroderma, and sarcoidosis. A number of circulating immune proteins are observed in these diseases that overlap with Resolaris activity. These include IP-10, MCP1, IL-8 and IL-6.

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

We are currently evaluating the most appropriate RPIC indication for the initial clinical evaluation of augmenting the Resokine pathway in lung via Resolaris. We are focusing on forms of ILD in which the lung involvement (and circulating biomarkers) appear to be amenable to the activities that we have observed for Resolaris preclinically or what we have gleaned from Jo-1 antibody patients. The initial trial in our clinical development plan in RPIC will evaluate the safety, tolerability, and biological and clinical activity of Resolaris in ILD patients and may use specific patterns of lung involvement by high resolution CT, or HRCT, to guide our efforts. In addition to safety measures, biological activity will likely be assessed by the monitoring of circulating cytokines such as IP-10, Il-6 and MCP-1. Clinical effects will be assessed thru several indices including pulmonary function tests, and measures of pulmonary gas exchange including diffusion capacity for the lung of carbon monoxide, or DLCO. We intend to initiate a clinical trial of Resolaris in a form of ILD in the first half of 2016. The data obtained in this initial ILD trial will inform further development of therapeutics leveraging the Resokine pathway in RPICs.

Our Preclinical Immuno-Modulatory Domain Program from the Resokine Pathway: iMod.Fc

We have initiated a discovery program to leverage our knowledge of the Resokine pathway to varying exposure and activity of the iMod domain through protein engineering. The program seeks to develop a potential therapeutic that we refer to as iMod.Fc, which would possess only the N-terminal immuno-modulatory activity of Resokine. We have conducted a series of experiments to understand how various product form modifications enhance exposure of the iMod domain. Fc fusion proteins have been successfully commercialized previously by others to enhance exposure while enabling biological activity. We explored this approach by fusing the immunoglobin Fc with one iMod domain, which can form a dimer. Enbrel and Zaltrap are commercialized examples of immunoglobulin Fc fusion proteins.

Our Fc fusion experiments have begun to delineate how to enhance the exposure of the iMod domain of Resokine while maintaining activity and provide insights into this domain harboring immuno-modulatory activity. Initial experiments have indicated that Fc fusion proteins can increase exposure and maintain iMod domain activity. We have generated results in a mouse model of lung inflammation and fibrosis for one iMod.Fc molecule that are encouraging. The increased exposure of this iMod.Fc allowed efficacy from a weekly dosing paradigm, as opposed to daily dosing, at a lower dose than needed for non-Fc fused Physiocrine controls.

Currently we are producing our iMod.Fc molecules in E. coli. This is in contrast to other marketed Fc fusion therapeutics that are manufactured in CHO cells.

Our Discovery Engine for Therapeutic Applications of Physiocrines: Lung and Liver Focused

We plan to leverage our discovery engine to identify other Physiocrine pathways of interest and select additional potential product candidates for preclinical and clinical investigation in a variety of disease settings. The engine that drives our discovery efforts is based on our scientific investigation of Physiocrine pathways and their proteins, coupled with a process of identifying disease indications that may benefit from a Physiocrine therapeutic. Through a combination of deep sequencing and bioinformatics panning, augmented by proteomic analysis, we identified over 300 naturally occurring Physiocrines. We then expressed and purified over 200 of these Physiocrines. Our strategy for identifying function and potential indications begins with developing a series of phenotypic assays for *in vitro* evaluations of function. Many of our purified Physiocrines were evaluated in numerous cell-based phenotypic assays that encompassed 14 distinct human cell types. In July 2014, a publication in *Science* described a portion of the results from our research, along with the research of our collaborators at Scripps La Jolla, Scripps Florida, Stanford University and the Hong Kong University of Science and Technology.

A key step in the discovery engine requires mining data from rare disease patients and linking this to the data generated in our phenotypic profiling experiments either *in vitro* or *in vivo*. For example, with HARS we studied published reports regarding Jo-1 antibody patients, also known as anti-synthetase patients. These clinical phenotypes led us to consider additional roles that extracellular HARS plays in muscle and lung. Thus, Resolaris, a HARS derivative, was evaluated in a number of *in vivo* pharmacology models that portray immune-driven inflammatory processes, including myopathy. The ability to restore homeostasis in multiple pharmacology models prompted us to catalog a number of rare myopathies that are immune driven as indications for therapeutic intervention with Resolaris.

We believe our strategy of understanding Physiocrine function by using *in vivo* experiments early and often while using patient data to focus this *in vivo* exploration has been validated by Resolaris. Additionally, we believe our discovery engine can be applied to other members of the Physiocrine class to help identify additional indications that may benefit from therapeutic intervention with Physiocrines.

We believe the biology of Physiocrines presents a novel protein therapeutic development opportunity based on the modulation of important physiological processes applicable to multiple diseases. This “pathway” approach or “physiology first” paradigm as we call it, which leverages the understanding of a basic physiological process,

has been used successfully to create some of the most important therapeutics in such diverse areas as oncology and ophthalmology. Given the breadth of our discoveries, we currently focus on Physiocrine pathways related to immune and regeneration responses to explore for product candidates with rare disease applications.

Discovery Programs in Lung and Liver

In addition, we believe some Physiocrine pathways may relate to fibrosis. Fibrosis is the formation of excess fibrous connective tissue in an organ or tissue in a reparative or reactive physiological process. Immune cells and their secreted molecules have been shown to play a critical role in the fibrotic process in a number of human tissues, including liver and lung. Persistent or unregulated inflammation is a hallmark of many chronic diseases, and is implicated in the development of fibrosis. Extracellular factors such as cytokines and chemokines act in the development of fibrosis by activating and recruiting inflammatory cells to developing fibrotic lesions.

As described previously, Resolaris had shown activity in *in vivo* pharmacology models of lung inflammation and pulmonary fibrosis. We are using this same model to evaluate other Physiocrine molecules in our pipeline. This coupled with ongoing functional knockout studies will be used to prioritize active Physiocrines and novel pathways for further studies.

Immune-mediated processes are also thought to be a driver in various forms of liver fibrosis. A connection between Physiocrines and fibrosis has also been demonstrated in functional knockout studies. In these experiments, conducted at aTyr, antibodies to individual mouse Physiocrines were induced in mice and the phenotypes related to the absence of the Physiocrine or blockade of its pathway were observed. Mice with antibodies to specific Physiocrines developed liver fibrosis and impaired liver function, as measured by decreased glycogen content, decreased albumin:globulin ratio and other functional features.

These experiments demonstrate that the blockade of Physiocrine pathways in rodents resulted in an *in vivo* phenotype characterized by immune cell infiltration or fibrotic disease in the lung or the liver. These data support the concept that Physiocrines may have the potential to inhibit, limit or otherwise regulate immune cell activity in both the lung and the liver, as well as the subsequent development of fibrosis in these tissues. Accordingly, we are continuing to investigate certain Physiocrines for potential therapeutic applications in both lung and liver indications.

Other Potential Discovery Programs

We have applied our discovery engine to identify a variety of medical conditions that we believe may be due to altered Physiocrine function, and are associated with mutations of members of the tRNA synthetase gene family, as set forth in the table below:

tRNA Synthetase Gene	Type of Mutation	Phenotype
AARS	Heterozygous (two forms)	CMT2N
	Heterozygous	Sporadic Axonal CMT
	Heterozygous	dHMN/CMT Variant
DARS	Compound Heterozygous	Hypomyelination
	Homozygous (two forms)	Hypomyelination
GARS	Heterozygous (three forms)	dSMA-V
	Heterozygous (two forms)	CMT2D/dSMA-V
	Heterozygous (two forms)	CMT2D
	Heterozygous (two forms)	CMT2
	Heterozygous	CMT2D/dHMN-V
	Heterozygous (three forms)	dHMN
	Compound Heterozygous	Non-Compaction Cardiomyopathy
HARS	Homozygous	Usher Syndrome
	Heterozygous	Peripheral Neuropathy
KARS	Compound Heterozygous	CMTRIB
	Homozygous (two forms)	Deafness
LARS	Homozygous	Infantile Liver Failure (ILFS1)
MARS	Compound Heterozygous	Infantile Liver Failure (ILFS2)
	Heterozygous	CMT2A1
	Compound Heterozygous	Hereditary Spastic Paraplegia
QARS	Compound Heterozygous (two forms)	Microcephaly
RARS	Compound Heterozygous (three forms)	Hypomyelination
YARS	Heterozygous (three forms)	DI-CMTC

Legend:

"_"ARS	=	"amino acid code" Aminoacyl tRNA synthetase. Alanine is represented by the letter A, hence alanine aminoacyl tRNA synthetase is abbreviated to AARS.
CMT	=	Charcot-Marie-Tooth Disease
CMT2A1	=	Charcot-Marie-Tooth Disease Type 2A1
CMT2D	=	Charcot-Marie-Tooth Disease Type 2D
CMT2N	=	Charcot-Marie-Tooth Disease Type 2N
CMTRIB	=	Intermediate Charcot-Marie-Tooth Disease B
dHMN	=	Distal Hereditary Motor Neuropathies
DI-CMTC	=	Intermediate Charcot-Marie-Tooth Disease C
dSMA-V	=	Distal Spinal Muscular Atrophy Type V

In addition, the following table summarizes research published regarding a variety of medical conditions that appear to be associated with autoantibodies targeting various tRNA synthetases (See Solomon, J., et al., (2011) Myositis-related interstitial lung disease and anti-synthetase syndrome, J. Bras. Pneumol. (2011) 37(1) 100-109):

tRNA synthetase target	Anti-tRNA synthetase antibody	# Patients Studied	% with Muscle Inflammation	% with Lung involvement
HARS	Jo-1	308	78-100	84
AARS	PL-12	69	60	95
TARS	PL-7	21	84	84
IARS	OJ	9	100	55
NARS	KS	6	0	100
GARS	EJ	1	100	100
FARSA, FARSB	ZO	1	100	100

Competition

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

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

In the area of RMICs, we expect to face competition from a number of companies, academic institutions and other organizations, including Akashi Therapeutics, Inc., BioMarin Pharmaceutical Inc., Catabasis Pharmaceuticals, Inc., FibroGen Inc., F. Hoffmann-La Roche AG, Milo Biotechnology, LLC., Nobelpharma Co.Ltd., Novartis AG, Pfizer, Inc., PTC Therapeutics, Inc., Sarepta Therapeutics, Inc. and Ultragenyx Pharmaceuticals, that are engaged in the clinical development of therapeutics to address muscle loss and muscle weakness in a variety of indications. More specifically, while there are currently no approved products for the treatment of FSHD, Acceleron Pharma Inc. is developing a clinical candidate, ACE-083, a locally acting protein therapeutic designed to increase muscle mass and strength in patients with neuromuscular disorders and other diseases characterized by a loss of muscle function, including FSHD. In addition, Facio Therapies recently announced its plans to screen chemical libraries to identify chemical compounds that will boost the expression of proteins known to repress one of the causal genes responsible for FSHD. In the area of LGMD, we are aware of a number of academic institutions engaged in the clinical development of therapeutics, including Genethon, a not-for-profit research laboratory created by the Association Française contre les Myopathies, or French Muscular Dystrophy Association, which has completed an experimental Phase 1 clinical trial in LGMD 2C using gene therapy; Nationwide Children's Hospital, which is currently conducting a Phase 1/2a clinical trial of an AAV vector to transport the alpha-sarcoglycan gene into muscles in in LGMD 2D; and NeuroGen Brain and Spine Institute in India, which is currently conducting a Phase 1 clinical trial in an unspecified form of LGMD using stem cell therapy.

In the area of RPICs, including ILD, we expect to face competition from pirfenidone, which is marketed by several companies worldwide, including InterMune Inc. (acquired by F. Hoffmann-La Roche AG Roche), Shionogi Ltd. and GNI Group Ltd., as well as nintedanib, a small molecule tyrosine-kinase inhibitor marketed

by Boehringer Ingelheim, both of which were approved by the FDA in October 2014. We are also aware of a number of companies engaged in the clinical development of therapeutics for lung diseases, including Astra Zeneca plc., Biogen Inc., Bristol-Myers Squibb, FibroGen Inc., Gilead Sciences Inc., Promedior, Inc. and Sanofi S. A.

Research and License Agreements

The Scripps Research Institute

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

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

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

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

Pangu Biopharma

In October 2007, we formed our Hong Kong subsidiary, Pangu BioPharma Limited, or Pangu BioPharma, a company registered in Hong Kong, to collaborate with the Hong Kong University of Science and Technology, or HKUST, on the discovery and development of aminoacyl tRNA synthetase protein therapeutics. We hold 98% of the outstanding shares of Pangu BioPharma, and a subsidiary of HKUST holds the remaining outstanding shares. Beginning in July 2008, Pangu BioPharma, in collaboration with HKUST, entered into a series of three research

grant agreements with the Government of the Hong Kong Special Administrative Region to carry out research in the discovery and development of Physiocrines. In December 2014, Pangu BioPharma renewed its annual joint research agreement with a subsidiary of HKUST, under which Pangu BioPharma agrees to fund research to be performed in 2015 under the agreement by the subsidiary of HKUST with respect to development of aminoacyl tRNA synthetase protein therapeutics. Pangu BioPharma is the sole beneficial owner of all resulting intellectual property rights from the research performed under these agreements, subject to the right of HKUST's subsidiary to use certain background intellectual property of HKUST in conducting the research and, in the event Pangu BioPharma applies for individual funding of any work under the research programs, compliance with the terms and conditions of any written agreement covering ownership of such funded works. Pangu BioPharma funds the annual research on a quarterly basis. Either party may terminate the agreement during the annual period upon an uncured breach of the agreement by the other party. We are also party to a license agreement with Pangu BioPharma, pursuant to which Pangu BioPharma has granted us an exclusive, royalty-bearing license (with a right to sublicense) in and to certain of Pangu BioPharma's solely and jointly owned patent rights and know-how to research, develop, manufacture, use, import, export, distribute, offer for sale, sell and have sold products incorporating such patent rights and know-how for any therapeutic, prognostic or diagnostic use throughout the world.

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. As of March 31, 2015, we own, or have exclusive licenses to, 24 issued U.S. and foreign patents and over 230 pending U.S. and foreign patent applications, with predicted expiration dates ranging from 2026 to 2034. In addition to patent protection, we also rely on trade secrets and careful monitoring of our proprietary information to protect aspects of our business that are not amenable to, or that we do not consider appropriate for, patent protection.

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

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

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

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

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

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

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

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

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

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is generally 20 years from the earliest date of filing the non-provisional patent application from which the patent issued.

In the United States, the patent term of a patent that covers a drug approved by the U.S. Food and Drug Administration, or FDA, may also be eligible for patent term extension, which permits patent term restoration as compensation for the patent term lost during the FDA regulatory review process. The Hatch-Waxman Act permits a patent term extension of up to five years beyond the expiration of the patent. The length of the patent term extension is related to the length of time the drug is under regulatory review. Patent extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval and only one patent applicable to an approved drug may be extended. Similar provisions are available in Europe and other non-United States jurisdictions to extend the term of a patent that covers an approved drug. In the future, if and when our pharmaceutical products receive FDA approval, we expect to apply for patent term extensions on patents covering those products. We intend to seek patent term extensions to any of our issued patents in any jurisdiction where these are available, however there is no guarantee that the applicable authorities, including the FDA in the United States, will agree with our assessment of whether such extensions should be granted, and even if granted, the length of such extensions.

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

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 facilities for the production of clinical quantities of our product candidates. We currently have no plans to build our own clinical or commercial scale manufacturing capabilities. The use of contracted manufacturing and reliance on collaboration partners is relatively cost-efficient and has eliminated the need for our direct investment in manufacturing facilities and additional staff early in development. Although we rely on contract manufacturers, we have personnel with extensive manufacturing experience to oversee our contract manufacturers.

Resolaris is produced in recombinant bacteria and then purified and packaged for clinical use. The active pharmaceutical ingredient for Resolaris is currently manufactured in India by Syngene International Limited, or Syngene, pursuant to a Master Services Agreement and a Quality Agreement executed in November 2012. We have a non-exclusive license to the cell line used to produce the active pharmaceutical ingredient for Resolaris. All other raw materials for Resolaris are commercially available. We intend to continue to work with Syngene for the production of Resolaris for preclinical studies and clinical testing up to pivotal trials. We contract with other third parties to conduct fill and finish and labeling, as well as for the storage and distribution of Resolaris to clinical sites and plan to do so for other product candidates that we may develop.

To date, our third-party manufacturers have met our manufacturing requirements for clinical development, and we expect that our current third-party manufacturers are capable of providing sufficient quantities of our product candidates to meet anticipated clinical development needs through to the start of the pivotal clinical trials.

To meet our projected needs for the pivotal clinical trials and larger scale commercial manufacturing, we are currently working with Fujifilm Diosynth Biotechnologies UK Limited and FDB USA, Inc., or Fujifilm, to

develop a scaled up manufacturing process for Resolaris. Additionally, we are currently negotiating with alternative fill-finish and labelling contract manufacturing organizations, or CMOs, to enable the commercial production and supply of Resolaris. We believe that Fujifilm and these alternative CMOs can satisfy our clinical, regulatory and commercial requirements for Resolaris. We cannot be certain, however, that the transfer and commercial scale up of the manufacturing process for Resolaris will not result in significant delay or add material additional costs.

Sales and Marketing

We currently intend to build the commercial infrastructure in the United States and Europe necessary to effectively support the commercialization of all 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. The commercial infrastructure for products directed at rare disease indications typically consists of a targeted, specialty sales force that calls on a limited and focused group of physicians supported by sales management, medical liaisons, internal sales support, an internal marketing group, and distribution support. One challenge unique to commercializing therapies for rare diseases is the difficulty in identifying eligible patients due to the very small and sometimes heterogeneous disease populations. Our management team is experienced in maximizing patient identification for both clinical development and commercialization purposes in rare diseases.

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

Although we currently intend to commercialize Resolaris and any other product candidates that we may develop on our own, we may elect in the future 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.

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, pricing, and export and import of pharmaceutical and biological products, such as those we are developing. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local, and foreign statutes and regulations require the expenditure of substantial time and financial resources.

U.S. Government Regulation

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

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

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

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

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

Clinical Trials

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

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

- *Phase 1*. The drug is initially introduced into healthy human subjects or patients with the target disease or condition. These studies are designed to evaluate the safety, dosage tolerance, metabolism and pharmacologic actions of the investigational new drug in humans, the side effects associated with increasing doses, and if possible, to gain early evidence on effectiveness.
- *Phase 2*. The drug is administered to a limited patient population to evaluate dosage tolerance and optimal dosage, identify possible adverse side effects and safety risks, and preliminarily evaluate efficacy.
- *Phase 3*. The drug is administered to an expanded patient population, generally at geographically dispersed clinical trial sites to generate enough data to statistically evaluate dosage, clinical effectiveness and safety, to establish the overall benefit-risk relationship of the investigational new drug product, and to provide an adequate basis for product approval.
- *Phase 4*. In some cases, the FDA may condition approval of a BLA or NDA for a product candidate on the sponsor's agreement to conduct additional clinical trials after approval. In other cases, a sponsor may voluntarily conduct additional clinical trials after approval to gain more information about the drug. Such post-approval studies are typically referred to as Phase 4 clinical trials.

A pivotal trial is a clinical trial that adequately meets regulatory agency requirements for the evaluation of a drug candidate's efficacy and safety such that it can be used to justify the approval of the product. Generally, pivotal trials are Phase 3 trials, but the FDA may accept results from Phase 2 clinical trials if the trial design provides a well-controlled and reliable assessment of clinical benefit, particularly in situations where there is an unmet medical need and the results are sufficiently robust.

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

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

Submission of a BLA or NDA to the FDA

Assuming successful completion of all required testing in accordance with all applicable regulatory requirements, detailed investigational new drug product information is submitted to the FDA in the form of a BLA or NDA requesting approval to market the product for one or more indications. Under federal law, the submission of most BLAs and NDAs is subject to an application user fee. For fiscal year 2015, the application user fee exceeds $2.3 million, and the sponsor of an approved BLA or NDA is also subject to annual product and establishment user fees, set at $110,370 per product and $569,200 per establishment. These fees are typically increased annually. Applications for orphan drug products are exempted from the BLA and NDA user fees and may be exempted from product and establishment user fees, unless the application includes an indication for other than a rare disease or condition.

A BLA or NDA must include all relevant data available from pertinent preclinical studies and clinical trials, including negative or ambiguous results as well as positive findings, together with detailed information relating

to the product's chemistry, manufacturing, controls, and proposed labeling, among other things. Data can come from company-sponsored clinical trials intended to test the safety and effectiveness of a use of a product, or from a number of alternative sources, including trials initiated by investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety and effectiveness of the investigational new drug product to the satisfaction of the FDA.

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

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

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

The FDA's Decision on a BLA or NDA

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

Expedited Review and Accelerated Approval Programs

A sponsor may seek approval of its product candidate under programs designed to accelerate FDA's review and approval of BLAs and NDAs. For example, Fast Track Designation may be granted to a drug intended for treatment of a serious or life-threatening disease or condition that has potential to address unmet medical needs for the disease or condition. The key benefits of fast track designation are more frequent interactions with the FDA during development and testing, the eligibility for priority review, and rolling review, which is submission of portions of an application before the complete marketing application is submitted. Based on results of the Phase 3 clinical trial(s) submitted in a BLA or NDA, upon the request of an applicant, the FDA may grant the

BLA or NDA a priority review designation, which sets the target date for FDA action on the application at six months after the FDA accepts the application for filing. Priority review is granted where there is evidence that the proposed product would be a significant improvement in the safety or effectiveness of the treatment, diagnosis, or prevention of a serious condition. If criteria are not met for priority review, the application is subject to the standard FDA review period of ten months after FDA accepts the application for filing. Priority review designation does not change the scientific/medical standard for approval or the quality of evidence necessary to support approval.

Under the accelerated approval program, the FDA may approve a BLA or NDA on the basis of either a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit, taking into account the severity, rarity, or prevalence of the condition and the availability or lack of alternative treatments. Post-marketing trials or completion of ongoing trials after marketing approval are generally required to verify the drug's clinical benefit in relationship to the surrogate endpoint or ultimate outcome in relationship to the clinical benefit. In addition, the Food and Drug Administration Safety and Innovation Act, or FDASIA, which was enacted and signed into law in 2012, established the new Breakthrough Therapy designation. A sponsor may seek FDA designation of its product candidate as a breakthrough therapy if the drug is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development.

Post-Approval Requirements

Drugs manufactured or distributed pursuant to FDA approvals are subject to pervasive and continuing regulation by the FDA, including, among other things, requirements relating to recordkeeping, periodic reporting, product sampling and distribution, advertising and promotion and reporting of adverse experiences with the product. After approval, most changes to the approved product, such as adding new indications or other labeling claims, are subject to prior FDA review and approval. There also are continuing, annual user fee requirements for any marketed products and the establishments at which such products are manufactured, as well as new application fees for supplemental applications with clinical data.

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

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

The FDA may withdraw approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown

problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution restrictions or other restrictions under a REMS program. Other potential consequences include, among other things:

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

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

Orphan Designation and Exclusivity

The FDA may grant orphan drug designation to drugs intended to treat a rare disease or condition that affects fewer than 200,000 individuals in the United States, or if it affects more than 200,000 individuals in the United States, there is no reasonable expectation that the cost of developing and making the drug for this type of disease or condition will be recovered from sales in the United States.

Orphan drug designation entitles a party to financial incentives such as opportunities for grant funding towards clinical trial costs, tax advantages, and user-fee waivers. In addition, if a product receives FDA approval for the indication for which it has orphan designation, the product is entitled to orphan drug exclusivity, which means the FDA may not approve any other application to market the same drug for the same indication for a period of seven years, except in limited circumstances, such as a showing of clinical superiority over the product with orphan exclusivity.

Pediatric Trials and Exclusivity

BLAs and NDAs must contain data, or a proposal for post-marketing activity, to assess the safety and effectiveness of an investigational new drug product for the claimed indications in all relevant pediatric populations in order to support dosing and administration for each pediatric subpopulation for which the drug is safe and effective. The FDA may, on its own initiative or at the request of the applicant, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults or full or partial waivers if certain criteria are met. Discussions about pediatric development plans can be discussed with the FDA at any time, but usually occur any time between the end-of-Phase 2 meeting and submission of the BLA or NDA. The requirements for pediatric data do not apply to any drug for an indication for which orphan designation has been granted.

Pediatric exclusivity is another type of non-patent exclusivity in the United States and, if granted, provides for the attachment of an additional six months of marketing protection to the term of any existing regulatory exclusivity, including the five-year and three-year non-patent and orphan exclusivity. This six-month exclusivity may be granted if a BLA or NDA sponsor submits pediatric data that fairly respond to a written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied;

rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of FDA-requested pediatric trials are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection covering the product are extended by six months. This is not a patent term extension, but it effectively extends the regulatory period during which the FDA cannot accept or approve another application relying on the BLA or NDA sponsor's data.

Patent Term Restoration

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

Biosimilars and Exclusivity

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

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

Abbreviated New Drug Applications for Generic Drugs

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

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

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

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

Hatch-Waxman Patent Certification and the 30-Month Stay

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

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

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

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

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

European Union/Rest of World Government Regulation

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

Whether or not we obtain FDA approval for a product, we must obtain the requisite approvals from regulatory authorities in foreign countries prior to the commencement of clinical trials or marketing of the product in those countries. Certain countries outside of the United States have a similar process that requires the submission of a clinical trial application much like the IND prior to the commencement of human clinical trials. In the European Union, for example, a clinical trial application, or CTA, must be submitted for each clinical protocol to each country's national health authority and an independent ethics committee, much like the FDA and IRB, respectively. Once the CTA is accepted in accordance with a country's requirements, the clinical trial may proceed.

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

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

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

Countries that are part of the European Union, as well as countries outside of the European Union, have their own governing bodies, requirements, and processes with respect to the approval of pharmaceutical and biologic products. If we fail to comply with applicable foreign regulatory requirements, we may be subject to, among other things, fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

Authorization Procedures in the European Union

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

- *Centralized procedure*. The EMA implemented the centralized procedure for the approval of human medicines to facilitate marketing authorizations that are valid throughout the European Economic Area, or EEA, which is comprised of the 28 member states of the European Union plus Norway, Iceland, and Lichtenstein. This procedure results in a single marketing authorization issued by the EMA that is valid across the EEA. The centralized procedure is compulsory for human medicines that are: derived from biotechnology processes, such as genetic engineering, contain a new active substance indicated for the treatment of certain diseases, such as HIV/AIDS, cancer, diabetes, neurodegenerative disorders or autoimmune diseases and other immune dysfunctions, and officially designated orphan medicines.
- For medicines that do not fall within these categories, an applicant has the option of submitting an application for a centralized marketing authorization to the European Commission following a

favorable opinion by the EMA, as long as the medicine concerned is a significant therapeutic, scientific or technical innovation, or if its authorization would be in the interest of public health.

- *National authorization procedures*. There are also two other possible routes to authorize medicinal products in several European Union countries, which are available for investigational medicinal products that fall outside the scope of the centralized procedure:
    - *Decentralized procedure*. Using the decentralized procedure, an applicant may apply for simultaneous authorization in more than one European Union country of medicinal products that have not yet been authorized in any European Union country and that do not fall within the mandatory scope of the centralized procedure.
    - *Mutual recognition procedure*. In the mutual recognition procedure, a medicine is first authorized in one European Union Member State, in accordance with the national procedures of that country. Following this, further marketing authorizations can be sought from other European Union countries in a procedure whereby the countries concerned agree to recognize the validity of the original, national marketing authorization.

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

New Chemical Entity Exclusivity

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

Orphan Designation and Exclusivity

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

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

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

Exceptional Circumstances/Conditional Approval

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

Accelerated Review

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

Pharmaceutical Coverage, Pricing and Reimbursement

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

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

The U.S. government, state legislatures and foreign governments have shown significant interest in implementing cost containment programs to limit the growth of government-paid health care costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. By way of example, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, collectively, the Healthcare Reform Law, 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. Adoption of government controls and measures, and tightening of restrictive policies in jurisdictions with existing controls and measures, could limit payments for pharmaceuticals.

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

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

Other Healthcare Laws and Compliance Requirements

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

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, to induce, or in return for, the purchase or recommendation of an item or service reimbursable under a federal healthcare program, such as the Medicare and Medicaid programs;
- federal civil and criminal false claims laws and civil monetary penalty laws, which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payors that are false or fraudulent;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, which created new federal criminal statutes that prohibit executing a scheme to defraud any healthcare benefit program and making false statements relating to healthcare matters;
- the federal transparency laws, including the federal Physician Payment Sunshine Act, that requires drug and biologics manufacturers to disclose payments and other transfers of value provided to physicians and teaching hospitals;
- HIPAA, as amended by the Health Information Technology and Clinical Health Act, or HITECH, and its implementing regulations, which imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information; and
- state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws that may apply to items or services reimbursed by any third-party payor, including commercial insurers,

and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

The Healthcare Reform Law 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, effective March 23, 2010. 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 Healthcare Reform Law provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act or the civil monetary penalties statute. Many states have adopted laws similar to the federal Anti-Kickback Statute, some of which apply to the referral of patients for healthcare items or services reimbursed by any source, not only the Medicare and Medicaid programs.

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

If our operations are found to be in violation of any of the laws described above or any other governmental regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, exclusion from participation in government healthcare programs, such as Medicare and Medicaid and imprisonment, damages, fines and the curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Our Advisors

Scientific Advisory Board

We have assembled a world-class scientific advisory board with expertise in biology for medical applications. The members of our scientific advisory board have made significant scientific contributions in their individual fields, have published in top-tier journals and have been recognized with numerous awards and distinctions, including the Nobel Prize in Physiology or Medicine. Members of our scientific advisory board provide strategic advice to us in such fields as proteomics, translational research and molecular biology, and perform such other services as may be mutually determined by us and the scientific advisory board member. Our scientific advisory board meets on an as-needed basis, based on our need for advice in their respective fields of expertise from time to time.

Name	Affiliation
Susan L. Ackerman, Ph.D.	Professor, The Jackson Laboratory and Howard Hughes Medical Institute Investigator
Bruce Beutler, M.D.	Founding Director, Center for the Genetics of Host Defense, UT Southwestern Medical Center
Floyd Bloom, M.D.	Professor Emeritus, Molecular and Cellular Neuroscience Department, The Scripps Research Institute
Benjamin F. Cravatt, Ph.D.	Professor and Chairman of the Department of Chemical Physiology, The Scripps Research Institute
Nancy Ip, Ph.D.	Dean of Science and Director of the State Key Laboratory of Molecular Neuroscience at Hong Kong University of Science and Technology
Osamu Nureki, Ph.D.	Professor, Department of Biological Sciences, Graduate School of Science, The University of Tokyo
Wing Hung Wong, Ph.D.	Stephen R. Pierce Family Goldman Sachs Professor in Science and Human Health; Professor of Statistics, Stanford University

Therapeutic Advisory Board

We have convened a select group of experienced drug discovery leaders to guide our discovery and development of innovative Physiocrine-based medicines. Our therapeutic advisory board members have extensive drug development expertise in both biotechnology company and pharmaceutical company settings. They have repeatedly demonstrated their ability to build high quality research and development organizations and to transform promising research into products. Members of our therapeutic advisory board provide strategic advice to us in the areas of translational and clinical research and perform such other services as may be mutually determined by us and the therapeutic advisory board member. Our therapeutic advisory board generally meets once per year.

Name	Affiliation
Thomas O. Daniel, M.D.	President, Research and Early Development, Celgene Corporation
R. Alan Ezekowitz, M.D., Ph.D.	Advisor, Cardinal Partners; President, Chief Executive Officer and Co-Founder, Abide Therapeutics, Inc.
L. Patrick Gage, Ph.D.	Chairman, Cytokinetics Inc.; Executive Chairman, Virdante Pharmaceuticals, Inc.
Richard Heyman, Ph.D.	Former Chief Executive Officer, Seragon Pharmaceuticals, Inc. (acquired by Genentech/Roche)
Keith James, Ph.D.	President, Ferring Research Institute Inc.; Senior Vice President, Research and Development, Ferring Pharmaceuticals Inc.
Paul Negulescu, Ph.D.	Vice President, Research, Vertex Pharmaceuticals Incorporated
Timothy Rink, MA., M.D., Sc.D.	Director, Kymab Ltd.; Director, Santhera Pharmaceuticals Holding AG; Director, Stevanage Bioscience Catalyst
Wendell Wierenga, Ph.D.	Director, Apricus Biosciences, Inc., Concert Pharmaceuticals, Inc. and Ocera Therapeutics, Inc.
Doug Williams, Ph.D.	Executive Vice President, Research and Development, Biogen Idec Inc.

Employees

As of April 1, 2015, we had 49 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.

Facilities

Our administrative offices and research laboratory are located in San Diego, California. We lease approximately 17,083 square feet of office and laboratory space under a lease that currently expires in May 2017. 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

We are not a party to any material legal proceedings at this time. From time to time, we may be subject to various legal proceedings and claims that arise in the ordinary course of our business activities. Although the results of litigation and claims cannot be predicted with certainty, as of the date of this prospectus, we do not believe we are party to any claim or litigation the outcome of which, if determined adversely to us, would individually or in the aggregate be reasonably expected to have a material adverse effect on our business. Regardless of the 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 information regarding our executive officers and directors, including their ages as of April 25, 2015:

Name	Age	Position
Executive Officers:		
John D. Mendlein, Ph.D.	55	Chief Executive Officer and Executive Chairman, Board of Directors
Frederic Chereau	48	President and Chief Operating Officer
David M. Weiner, M.D.	50	Chief Medical Officer
Melissa A. Ashlock, M.D.	57	Vice President, External Scientific Alliances and Human Genetics
John C. McKew, Ph.D.	51	Vice President, Research
Fred Ramsdell, Ph.D.	54	Vice President, Immunology
Kelly Blackburn	51	Vice President, Clinical Affairs
Andrew Cubitt, Ph.D.	52	Vice President, Product Protection
Holly D. Chrzanowski	49	Vice President, Enterprise Talent and Organization
Marcy Graham	48	Vice President, Investor Relations and Corporate Communications
Non-Management Directors:		
John K. Clarke (1) (3)	61	Chairman of the Board
Srinivas Akkaraju, M.D., Ph.D. (2)	47	Director
James C. Blair, Ph.D. (2) (3)	75	Director
Kathryn E. Falberg (1) (3)	54	Director
Mark Goldberg, M.D.	60	Director
Amir H. Nashat, Sc.D. (1)	42	Director
Paul Schimmel, Ph.D. (2)	74	Director

(1) Member of the audit committee.
(2) Member of the compensation committee.
(3) Member of the nominating and corporate governance committee.

John D. Mendlein, Ph.D. has served as our Executive Chairman since July 2010 and as our Chief Executive Officer since September 2011. Dr. Mendlein is Vice Chairman of the Board of Fate Therapeutics, Inc., a biopharmaceutical company, and also holds board positions with Moderna Therapeutics, Inc., Pronutria Biosciences, Inc. and BIO (Biotechnology Industry Organization) emerging companies board. Dr. Mendlein previously served as the Chief Executive Officer of Adnexus Therapeutics, Inc., a biopharmaceutical company, from 2005 to 2008, which was purchased by Bristol-Myers Squibb Company in 2008. Dr. Mendlein also served on the board of directors of Monogram Biosciences, Inc., an HIV and oncology diagnostic company that was acquired by Laboratory Corporation of America Holdings in 2009. Before that, he served as Chairman and Chief Executive Officer of Affinium Pharmaceuticals, Ltd. (acquired by Debiopharm Group) from 2000 to 2005, and as a board member, General Counsel and Chief Knowledge Officer at Aurora Bioscience Corporation (acquired by Vertex Pharmaceuticals) from August 1996 to September 2001. Dr. Mendlein holds a Ph.D. in physiology and biophysics from the University of California, Los Angeles, a J.D. from the University of California, Hastings College of the Law, and a B.S. in biology from the University of Miami. Dr. Mendlein is the co-author or co-inventor of over 210 publications and published patent properties, including a number of patents associated with our company.

Frederic Chereau has served as our President and Chief Operating Officer since January 2014. From September 2012 to December 2013, Mr. Chereau was Senior Vice President, Global Angioedema Franchise Lead at Shire plc, a global biopharmaceuticals company. Prior to that, from October 2008 to September 2012, he served as President and Chief Executive Officer of Pervasis Therapeutics, Inc., a clinical-stage therapeutics

company where substantially all assets were acquired by Shire plc. Before Pervasis, Mr. Chereau worked at Genzyme from 1999 to 2008, where he held various roles, including Vice President and General Manager of the Cardiovascular Business Unit. Prior to that, he started his career at Hemotech S.A., where he held sales and marketing roles. Mr. Chereau sits on the Advisory Board of Cell2B, a biotechnology company dedicated to the development of advanced cellular therapies in Portugal, and on the Strategic Advisory Board of La Rochelle Business School in France. Mr. Chereau holds a B.S. in physics from the University of Paris, a Master in Management from La Rochelle Business School in France and an M.B.A. from INSEAD, Fontainebleau, France and Singapore.

David M. Weiner, M.D. has served as our Chief Medical Officer since March 2014. Prior to that, he served as the Chief Medical Officer of Proteostasis Therapeutics, Inc., a venture backed biopharmaceutical company, from September 2012 to March 2014, and as its interim Chief Executive Officer from July 2013 to March 2014. From 2007 to 2011, Dr. Weiner held a number of roles, including Vice President and head of early clinical development, Neurodegenerative Disease, at Merck Serono S.A., a global pharmaceutical company. From 1997 to 2007, he served in both pre-clinical and clinical development roles at ACADIA Pharmaceuticals. Dr. Weiner's clinical experience includes a faculty appointment in Neuroscience and Psychiatry at the University of California, San Diego. He trained in neurology at New York Hospital, Memorial Sloan Kettering Cancer Center, Weill Cornell Medical Center, after completing a medical internship at St. Vincent's Medical Center in New York. Dr. Weiner holds a B.A. in biopsychology from Brandeis University and an M.D. from the State University of New York at Buffalo. Dr. Weiner is the co-author or co-inventor of over 30 publications and patent properties, and serves on the advisory board of the Michael J. Fox Foundation. He also holds licenses to practice medicine (States of California, New York and Vermont).

Melissa A. Ashlock, M.D. has served as our Vice President, External Scientific Alliances and Human Genetics since May 2011. Between 1999, and 2011, Dr. Ashlock was employed by the Cystic Fibrosis Foundation (CFF), holding positions including Vice President of Drug Discovery for its therapeutics affiliate where she was the program leader for multiple CFF funded collaborative drug discovery programs with industry. Among these was a multi-year collaboration with Vertex that led to the worldwide marketed CFTR modulator, Kalydeco. Dr. Ashlock has also held consultancy roles with following companies: Vertex Pharmaceuticals Incorporated, a global biotechnology company, from March 2011 to June 2011; John J. Flatley Company (for their cystic fibrosis research lab), from January 2011 to June 2011; Galapagos NV, a clinical-stage biotechnology company, from April 2010 to April 2011; and Therapeutics for Rare and Neglected Diseases Program, National Institutes of Health, from March 2009 to February 2010. She completed her internship and medical residency in adult internal medicine at New York Hospital (Cornell University Medical College) and Mary Hitchcock Memorial Hospital (Dartmouth Medical School), respectively. Dr. Ashlock, who has also published under the name Melissa Rosenfeld, M.D., has been co-inventor or author of more than 50 issued patents and publications. Dr. Ashlock holds a B.S. in biochemistry from Purdue University and an M.D. from Weill Cornell Medical College. She also holds a license to practice medicine (State of Maryland).

John C. McKew, Ph.D. has served as our Vice President, Research since October 2014. Prior to that, from October 2010 to October 2014, Dr. McKew served as the Acting Scientific Director of the Division of Preclinical Innovation at the National Center for Advancing Translational Sciences (NCATS) within the National Institutes of Health (NIH). A portion of his responsibilities were focused on building the Therapeutics for Rare and Neglected Diseases and the Bridging Interventional Developments Gaps programs into novel collaborative preclinical and early clinical development programs. Before joining the NIH, from October 1993 to January 2011, Dr. McKew held a director level position at Wyeth Research in Cambridge, Massachusetts. Dr. McKew held post-doctoral research positions at the University of Geneva and Firmenich, SA and is currently an Adjunct Associate Professor at the Boston University School of Medicine. He has given more than 60 invited lectures, and is an author on over 45 peer-reviewed articles and an inventor on more than 35 patents and patent applications. He holds B.S. degrees in chemistry and biochemistry from the State University of New York at Stony Brook and a Ph.D. in chemistry from the University of California, Davis.

Fred Ramsdell, Ph.D. has served as our Vice President, Immunology since June 2014. He also provides consulting services to a number of biotechnology and pharmaceutical companies, as well as to various non-profit organizations in the area of immunobiology. Prior to joining aTyr, from October 2008 to May 2014, Dr. Ramsdell served as Scientific Director, Discovery Immunology at Novo Nordisk, A/S, a global healthcare company. Dr. Ramsdell was Director of the Immunology Program at Darwin Molecular Corporation (acquired by Celltech Limited) from 1994 to 2004. Prior to that, he worked as a Senior Scientist at Immunex Corporation. He conducted post-doctoral studies at the National Institutes of Health, researching a variety of questions regarding immune cell function and tolerance. He has over 50 publications. He holds a B.S. in biochemistry and cell biology from the University of California, San Diego and a Ph.D. in microbiology and immunology from the University of California, Los Angeles.

Kelly Blackburn has served as our Vice President, Clinical Affairs since July 2013. Ms. Blackburn served as a consultant from September 2012 to July 2013 to a number of companies, including Agios Pharmaceuticals, Promedior Inc. and aTyr. Prior to this, Ms. Blackburn was the Vice President, Clinical Development Operations at Vertex Pharmaceuticals Incorporated from September 2006 to September 2012. In this role she oversaw the global operations through to NDA for Kalydeco and Incivek. From September 2002 to August 2006, Ms. Blackburn was Director of Clinical and Safety Operations for Millennium Pharmaceuticals where she was responsible for the VELCADE program which was successfully approved during her tenure. Ms. Blackburn has also served as an advisor to Transforme1, a new technology company for data capture, from July 2013 to December 2014. Ms. Blackburn holds a B.S. in biochemistry from University of New Hampshire, an M.H.A. from Quinnipiac College and an M.Ed. from Cambridge College.

Andrew Cubitt, Ph.D. has served as our Vice President, Product Protection since September 2011 and provided consulting services to us from January 2011 to September 2011. Prior to that, from 2009 to 2011, he worked as a senior patent agent for the Global Patent Group LLC, a patent consulting firm. He co-founded Anaptys Biosciences, a therapeutic antibody company, in 2005 and served as Executive Director of Corporate Development until 2009. He also served as Senior Manager, Technology and Intellectual Property at Aurora Bioscience Corporation. Dr. Cubitt did his postdoctoral training at Weill Cornell Medical College in New York, and at the University of California San Diego, where he was part of team that initiated development of the green fluorescent protein (GFP) with Roger Tsien, Ph.D. Dr. Cubitt holds a Ph.D. in biochemistry from the University of Sheffield and a first class honors degree (B.Sc) in medical biochemistry from the University of Birmingham in the UK. Dr Cubitt is a co-inventor or co-author of 18 issued US patents and 20 publications.

Holly D. Chrzanowski has served as our Vice President, Enterprise Talent and Organization since April 2013 and provided consulting services to us from 2010 to 2013. Prior to joining aTyr, she operated her own human resources consulting practice, HC Consulting, for 12 years, providing human resources consulting services to a wide variety of biotechnology companies located nationwide. She also served as a Director, Human Resources at Vertex Pharmaceuticals Incorporated as a consultant and Senior Manager, Human Resources at Aurora Biosciences Corporation. Prior to this, Ms. Chrzanowski held a variety of management level positions in human resources at Geometric Results Incorporated, a multinational subsidiary of Ford Motor Company (acquired by MSX International). Ms. Chrzanowski attended the University of Salzburg, Austria where she studied German language. She holds a B.A. in political science from California State University at Long Beach.

Marcy Graham has served as our Vice President, Investor Relations and Corporate Communications since January 2015. Prior to that, from 2013 to 2015, Ms. Graham served as head of Investor Relations and Corporate Communications at Ambit Biosciences (acquired by Daichi Sankyo), a biopharmaceutical company. Before joining Ambit, from 2011 to 2013, Ms. Graham served as Senior Director, Investor Relations and Corporate Communications at Sequenom, Inc., a life sciences diagnostics company. Prior to Sequenom, from 2007 to 2011, she was the Executive Director, Investor Relations at Genoptix, Inc. and was previously the Director of Investor Relations at Novatel Wireless following a position heading the Investor Relations effort at Leap Wireless, home of wireless telecommunications provider Cricket Communications. Ms. Graham holds a

Certification in Investor Relations from the University of California, Irvine, an M.B.A. from the Robert O. Anderson School of Management at the University of New Mexico and a B.A. degree in Journalism and Mass Communications from the University of New Mexico.

John K. Clarke has served as Chairman of our Board of Directors since September 2005. Mr. Clarke is Managing General Partner of Cardinal Partners, a venture capital partnership 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 Chairman of the Board of Directors of Alnylam Pharmaceuticals, Inc. and as a director of Momenta Pharmaceuticals, Inc. and Rib-X Pharmaceuticals Inc. He has also served as a director for Verastem, Inc., Sirtris Pharmaceuticals, Inc. (acquired by GlaxoSmithKline), TechRx Technology Services Corporation (acquired by NDCHealth) and Visicu, Inc. (acquired by Phillips Electronics). 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. We believe 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.

Srinivas Akkaraju, M.D., Ph. D. Dr. Akkaraju has served as a director since March 2015. Since April 2013, Dr. Akkaraju has been General Partner of Sofinnova Ventures. From January 2009 to April 2013, Dr. Akkaraju served as Managing Director of New Leaf Venture Partners. From August 2006 to December 2008, Dr. Akkaraju served as a Managing Director at Panorama Capital, LLC, a private equity firm founded by the former venture capital investment team of J.P. Morgan Partners, LLC, a private equity division of JPMorgan Chase & Co. Prior to co-founding Panorama Capital, he was with J.P. Morgan Partners, which he joined in April 2001 and of which he became a Partner in January 2005. From October 1998 to April 2001, he was in Business and Corporate Development at Genentech, Inc. (now a member of the Roche Group), a biotechnology company, most recently as Senior Manager. In addition to aTyr, Dr. Akkaraju serves as a director of Seattle Genetics, Intercept Pharmaceuticals, Inc., ZS Pharma, and Versartis, Inc, which are all publicly traded biotechnology companies. Previously, Dr. Akkaraju served as a director on the boards of Barrier Therapeutics, Inc., Eyetech Pharmaceuticals, Inc. and Synageva Biopharma Corp., all publicly traded biotechnology companies, and Amarin Corporation plc, a foreign publicly traded biotechnology company. Prior to joining Genentech, Dr. Akkaraju was a graduate student at Stanford University, where he received an M.D. and a Ph.D. in Immunology. He holds B.A.s in biochemistry and computer science from Rice University. We believe that Dr. Akkaraju is qualified to serve on our board of directors due to his strong scientific background coupled with extensive experience in private equity and venture capital investing allowing him to thoroughly understand our technology and provide strong business and strategic expertise.

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., as well as numerous private company boards. He previously served on the boards of Zogenix, Inc., Cadence Pharmaceuticals, Inc. and Five Prime Therapeutics, Inc. Dr. Blair currently serves on the board of directors of the Prostate Cancer Foundation and the Sanford-Burnham Medical Research Institute. He is also on the advisory boards of the Department of Molecular Biology at Princeton University, the USC Stevens Institute for Innovation, and the Division of Chemistry and Chemical Engineering at the California Institute of Technology. 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. We believe 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.

Kathryn E. Falberg has served as a director since July 2014. Ms. Falberg most recently served as Executive Vice President and Chief Financial Officer of Jazz Pharmaceuticals PLC, a biopharmaceutical company, from 2009 to 2014. From 1995 to 2001, Ms. Falberg was with Amgen Inc., where she served as Senior Vice President, Finance and Strategy, Chief Financial Officer, and before that as Vice President, Controller and Chief Accounting Officer, and Vice President, Treasurer. Ms. Falberg currently serves as Chairman of the board of directors and is the Audit Committee Chair of Halozyme Therapeutics, Inc., a biopharmaceutical company, and Medivation, Inc., a

biopharmaceutical company. Ms. Falberg holds a B.A. in economics and an M.B.A. in finance from the University of California, Los Angeles. We believe Ms. Falberg is qualified to serve on our board of directors due to her extensive background in financial and accounting matters for public companies and her leadership experience in the biotechnology industry.

Mark Goldberg, M.D. has served as a director since April 2015. Dr. Goldberg served as Executive Vice President, Medical and Regulatory Strategy for Synageva BioPharma Corp., a biopharmaceutical company, from January to September 2014. Prior to that he served as Senior Vice President, Medical and Regulatory Strategy for Synageva from 2011 to January 2014. Effective September 22, 2014, Dr. Goldberg remained an employee of Synageva contributing to medical and regulatory strategy, but ceased to be an officer of the company. Prior to joining Synageva he served in various management capacities of increasing responsibility at Genzyme Corporation, a biopharmaceutical company, from 1996 to 2011, most recently as Senior Vice President, Clinical Research and Therapeutic Group Head for Oncology, Genetic and Neurodegenerative Diseases Clinical Development, and as Chairman of Genzyme's Early Product Development Board. Prior to joining Genzyme he was a full-time staff physician at Brigham and Women's Hospital and the Dana-Farber Cancer Institute, where he still holds appointments. Dr. Goldberg is an Associate Professor of Medicine at Harvard Medical School. Dr. Goldberg holds a Doctor of Medicine degree from Harvard Medical School. Dr. Goldberg is also a director of GlycoMimetics, Inc., ImmunoGen, Inc. and Idera Pharmaceuticals, Inc. and, within the past five years, he also served as a director of Synageva. We believe Dr. Goldberg is qualified to serve on our board of directors due to his extensive experience in clinical research, his medical background and his public company board experience.

Amir H. Nashat, Sc.D. has served as a director since November 2006. He is also a Managing General Partner at Polaris Venture Partners, a venture capital firm. He joined Polaris in April 2002 and focuses on investments in healthcare, consumer products and energy. Dr. Nashat is currently a director of Fate Therapeutics, Inc. and BIND Therapeutics, Inc., as well as a director of several private companies. Additionally, Dr. Nashat has served as a director of Adnexus Therapeutics, Inc. (acquired by Bristol-Myers Squibb Company) and other private companies. Dr. Nashat holds a Sc.D. in chemical engineering from the Massachusetts Institute of Technology with a minor in biology and an M.S. and B.S. in materials science and mechanical engineering from the University of California, Berkeley. We believe Dr. Nashat is qualified to serve on our board of directors due to his extensive experience within the field of drug discovery and development, his broad leadership experience on various boards, and his financial expertise with life sciences companies.

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. Dr. Schimmel is an Ernest and Jean Hahn Professor at The Skaggs Institute for Chemical Biology at The Scripps Research Institute. 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. in biochemistry and biophysics from Ohio Wesleyan University and a Ph.D. from the Massachusetts Institute of Technology. We believe 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 Physiocrine biology and other areas important to the development of therapeutics.

Principal Financial and Accounting Officer

Below is the biography of Stan Blackburn, our principal financial and accounting officer, who serves as a consultant:

Stan Blackburn has served as our Acting Chief Financial Officer as a consultant since October 2008. Mr. Blackburn has provided senior financial consulting services to early stage life science and technology companies through his firm BlackFord Partners, Inc. for over 13 years and as an independent consultant for over 25 years. He worked as a certified public accountant with Arthur Andersen & Company for over nine years. He holds a B.S. in accountancy from the University of Illinois.

Composition of Our Board of Directors

Our board of directors currently consists of eight members, all of whom were elected pursuant to the provisions of a stockholders' agreement, which will terminate immediately prior to the completion of this offering. Pursuant to the provisions of a registration and voting rights agreement, upon the completion of this offering, certain of our stockholders who previously held shares of our Series E redeemable convertible preferred stock may designate one individual as a nominee to serve on our board of directors, subject to certain conditions. Our nominating and corporate governance committee and board of directors may consider a broad range of factors relating to the qualifications and background of director nominees, which may include diversity and is not limited to race, gender or national origin. We have no formal policy regarding board diversity. Our nominating and corporate governance committee's and board of directors' priority in selecting board members is identification of persons who will further the interests of our stockholders through his or her established record of professional accomplishment, the ability to contribute positively to the collaborative culture among board members, knowledge of our business, understanding of the competitive landscape and professional and personal experiences and expertise relevant to our business strategy. Our directors hold office until their successors have been elected and qualified or until the earlier of their resignation or removal.

Our amended and restated certificate of incorporation and amended and restated bylaws that will become effective upon the completion of this offering also provide that our directors may be removed only for cause by the affirmative vote of the holders of at least 75% of the votes that all our stockholders would be entitled to cast in an annual election of directors, and that any vacancy on our board of directors, including a vacancy resulting from an enlargement of our board of directors, may be filled only by vote of a majority of our directors then in office.

Director Independence. Our board of directors has determined that all members of our board of directors, except Dr. Mendlein, are independent, as determined in accordance with the rules of The NASDAQ Stock Market and the Securities and Exchange Commission, or SEC. In making such independence determination, our board of directors considered the relationships that each non-employee director has with us and all other facts and circumstances that our 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 five percent of our common stock. Upon the completion of this offering, we expect that the composition and functioning of our board of directors and each of our committees will comply with all applicable requirements of The NASDAQ Stock Market and the rules and regulations of the SEC. There are no family relationships among any of our directors or executive officers.

Staggered Board. In accordance with the terms of our amended and restated certificate of incorporation and amended and restated bylaws that will become effective upon the completion of this offering, our board of directors will be divided into three classes, Class I, Class II and Class III, with each class serving staggered three-year terms. Upon the expiration of the term of a class of directors, directors in that class will be eligible to be elected for a new three-year term at the annual meeting of stockholders in the year in which their term expires.

- Our Class I directors will be Mr. Clarke, Dr. Nashat and Dr. Schimmel;
- Our Class II directors will be Dr. Mendlein, Ms. Falberg and Dr. Blair; and
- Our Class III directors will be Dr. Akkaraju and Dr. Goldberg.

Our amended and restated certificate of incorporation and amended and restated bylaws that will become effective upon the completion of this offering provide that the authorized number of directors may be changed only by resolution of our board of directors.

The division of our board of directors into three classes with staggered three-year terms may delay or prevent stockholder efforts to effect a change of our management or a change in control.

Leadership Structure of the Board

Our board of directors believes that the decision as to who should serve as Chairman, Executive Chairman and Chief Executive Officer is the proper responsibility of the board of directors. Our amended and restated bylaws that will be in effect upon the completion of this offering will not require our Executive Chairman, Chairman and Chief Executive Officer positions to be separate and our board of directors will carefully consider the advantages and disadvantages of such separation or combination. At the present time, our board of directors believes the interests of all stockholders are best served through a leadership model with a combined Executive Chairman and Chief Executive Officer position and an independent Chairman. Our Executive Chairman and Chief Executive Officer focuses on our day-to-day operations, while our independent Chairman serves as our lead independent director. Our independent Chairman leads our board of directors in its fundamental role of providing advice to and independent oversight of management.

Board's Role in Risk Oversight

We face a number of risks, including risks relating to our financial condition, development and commercialization activities, operations and intellectual property as more fully discussed under "Risk Factors" in this prospectus. 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 our 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.

Board Committees

Our board of directors has established an audit committee, a compensation committee and a nominating and governance committee. The composition of each committee set forth below became effective upon the effectiveness of the registration statement of which this prospectus forms a part. Each committee will operate under a charter approved by our board. Following this offering, copies of each committee's charter will be posted on the Corporate Governance section of our website, at www.atyrpharma.com.

Audit Committee

Mr. Clarke, Ms. Falberg and Dr. Nashat currently serve on the audit committee, which is chaired by Ms. Falberg. Our board of directors has determined that each of Mr. Clarke, Ms. Falberg and Dr. Nashat is an independent director under the NASDAQ Marketplace Rules and Rule 10A-3 of the Securities Exchange Act of 1934, as amended, or the Exchange Act. We believe that the composition of our audit committee will comply with applicable rules of The NASDAQ Stock Market under the phase-in schedule described above. Our board of directors has designated Ms. Falberg as an "audit committee financial expert," as defined under the applicable rules of the Securities and Exchange Commission. 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.

Compensation Committee

Dr. Akkaraju, Dr. Blair and Dr. Schimmel currently serve on the compensation committee, which is chaired by Dr. Blair. Our board of directors has determined that each member of the compensation committee is "independent" as that term is defined in the applicable NASDAQ Stock Market rules. 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 determining the compensation of our Chief Executive Officer;
- reviewing and approving the compensation of our other officers;
- reviewing and establishing our overall management 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 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 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.

Nominating and Corporate Governance Committee

Dr. Blair, Mr. Clarke and Ms. Falberg currently serve on the nominating and corporate governance committee, which is chaired by Mr. Clarke. Our board of directors has determined that each member of the nominating and corporate governance committee is "independent" as that term is defined in the applicable NASDAQ Stock Market rules. The nominating and corporate governance committee's responsibilities include:

- developing and recommending to our 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 our board of directors;
- recommending to our board of directors the persons to be nominated for election as directors and to each of our board's committees;
- developing and recommending to our board of directors a set of corporate governance guidelines; and
- overseeing the evaluation of our board of directors and management.

Our board of directors may establish other committees from time to time.

Compensation Committee Interlocks and Insider Participation

None of the members of our compensation committee has at any time during the prior three years been one of our officers or employees. None of our executive officers currently serves, or in the past fiscal year has served, as a member of our board of directors or compensation committee of any entity that has one or more executive officers serving on our board of directors or compensation committee.

Corporate Governance

In connection with this offering, we have adopted a written code of business conduct and ethics that applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. Following the completion of this offering, a current copy of the code will be posted on the Corporate Governance section of our website, which is located at www.atyrpharma.com. If we make any substantive amendments to, or grant any waivers from, the code of business conduct and ethics for any officer or director, we will disclose the nature of such amendment or waiver on our website or in a current report on Form 8-K.

EXECUTIVE AND DIRECTOR COMPENSATION

Summary Compensation Table

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, 2014 and our two other most highly compensated executive officers who were serving as executive officers as of December 31, 2014. We refer to these officers as our named executive officers.

Name and Principal Position	Year	Salary ($)	Stock Awards ($)	Option Awards ($)(1)	Non-Equity Incentive Plan Compensation ($)(2)	All Other Compensation ($)(3)	Total ($)
John D. Mendlein, Ph.D *Chief Executive Officer and Executive Chairman*	2014	410,000	268,089(4)	604,606(5)	76,875	38,407	1,397,977
	2013	400,000	—	408,959	160,000	—	968,959
Frederic Chereau *President and Chief Operating Officer*	2014	319,731(6)	—	1,503,835	49,140	149,511	2,022,217
David M. Weiner, M.D. *Chief Medical Officer*	2014	265,208(7)	—	1,470,231	31,280	75,207	1,841,926

(1) In accordance with SEC rules, this column reflects the aggregate grant date fair value of the option awards granted during the years indicated, computed in accordance with Financial Accounting Standard Board ASC Topic 718 for stock-based compensation transactions, or ASC 718. Assumptions used in the calculation of these amounts are included in Note 7 to our consolidated financial statements included elsewhere in this prospectus. These amounts do not reflect the actual economic value that will be realized by the named executive officer upon the vesting of the stock options, the exercise of the stock options or the sale of the common stock underlying such stock options.

(2) The amounts reported reflect the discretionary cash bonus determined by our board of directors upon recommendation of our compensation committee based on achievement of certain performance goals and metrics as specified by our board of directors upon recommendation of our compensation committee.

(3) The amounts reported in this column include (i) supplemental compensation paid to Dr. Mendlein and Mr. Chereau in the amounts of $28,407 and $21,067, respectively, (ii) reimbursements to Dr. Mendlein pursuant to his employment agreement for medical expenses in the amount of $10,000, (iii) contributions made by the Company to a health savings account for Mr. Chereau in the amount of $2,275, (iv) relocation expenses for Mr. Chereau and Dr. Weiner, in the amounts of $81,000 and $50,000, respectively and (v) related tax gross-ups for the relocation expenses of Mr. Chereau and Dr. Weiner, of $45,169 and $25,207, respectively.

(4) In accordance with SEC rules, this amount reflects the incremental grant date fair value, computed as of the modification date in accordance with ASC 718 associated with the amendment in December 2014 of a restricted stock grant to provide for the lapsing of the Company's right of repurchase with respect to 24,247 shares of common stock underlying the grant. This amount was not paid to or realized by the officer in the year indicated.

(5) The amount reported also reflects the incremental grant date fair value of $453,452, computed as of the modification date in accordance with ASC 718, associated with the amendment in December 2014 of the vesting schedule for a previously granted stock option. Assumptions used in the calculation of this amount are included in Note 7 to our consolidated financial statements included elsewhere in this prospectus. This amount was not paid to or realized by the officer in the year indicated.

(6) Mr. Chereau began his employment with us on January 9, 2014.

(7) Dr. Weiner began his employment with us on March 17, 2014.

Employment Arrangements with Our Named Executive Officers

John D. Mendlein, Ph.D.

Dr. Mendlein entered into an at-will employment agreement with us as of January 1, 2010, which provided for an initial annual base salary of $150,000, subject to periodic review and increases as determined by our board of directors. Pursuant to the terms of his employment agreement, Dr. Mendlein is considered annually for a bonus target, currently in an amount of up to 50% of his then-current base salary, as determined by our board of directors and compensation committee. Dr. Mendlein may elect to receive a grant of fully-vested shares of our common stock in lieu of a cash bonus. In connection with commencement of his employment, we granted Dr. Mendlein a signing bonus of $31,250. In addition, Dr. Mendlein is entitled to reimbursement in an amount up to $10,000 per calendar year of certain healthcare fees and expenses.

Payments in Connection with a Change of Control

Upon the completion of this offering, Dr. Mendlein will be entitled to request an agreement with us regarding a change in control that would provide for a "gross-up" payment in the event certain excise taxes and penalties are imposed as a result of Sections 280G and/or 4999 of the Code. In the event that Dr. Mendlein's employment ends within 12 months of any change of control as defined in the agreement, other than as a result of termination for cause, we have agreed to enter into a consulting or advisory relationship with Dr. Mendlein following such change of control such that any options or restricted shares that were unvested as of the consummation of such change of control become fully vested, subject to Dr. Mendlein continuing to provide bona fide services to the Company.

Payments Provided upon Termination for Good Reason or Without Cause

Dr. Mendlein's employment is at-will. In the event of termination by Dr. Mendlein for good reason or by us without cause, Dr. Mendlein will be entitled to receive (i) the amount of his accrued but unpaid salary, earned but unpaid bonus, and any accrued but unused vacation as of the date of termination, (ii) reimbursement of any expenses properly incurred on behalf of the Company prior to any such termination and not yet reimbursed, (iii) continuation of his base salary for a period of six months after the effective date of termination and one half of the full bonus that Dr. Mendlein would have received had the Company met all of the targets in the annual bonus plan that was approved by our board for the calendar year in which the termination occurred, and (iv) continuation of group health plan benefits for a period of six months, in the case of each of (iii) and (iv), subject to the execution and non-revocation of a release agreement and written acknowledgement of Dr. Mendlein's continuing confidentiality obligations.

Under Dr. Mendlein's employment agreement, the terms below are generally defined as follows:

"cause" means (i) conduct constituting an uncured material act of willful misconduct in connection with the performance of his duties; (ii) conviction of, or entry of a pleading of guilty or nolo contendere to, any crime involving fraud or embezzlement that results in material damage to the Company or any felony; (iii) willful and repeated failure to substantially perform the duties, functions and responsibilities of the position that results in material damage to the Company that continues uncured for 30 days after prior written notice; (iv) a material breach of any of the material provisions of his employment agreement that is uncured for 30 days after prior written notice; or termination in connection with the bankruptcy, dissolution, liquidation, winding up, assignment for the benefit of creditors, or other cessation of the business of the Company as a going concern, other than to effectuate a change of control; and

"good reason" means (i) a substantial diminution or other substantive adverse change, not consented to by Dr. Mendlein, in the nature of scope of his responsibilities, authorities, powers, function or duties; (ii) an involuntary reduction in his base salary except for a decrease as part of reductions by the Company of the annual base salary of its executive employees generally; (iii) a breach by the Company of any of its material obligations under any agreement between the Company and Dr. Mendlein that remains uncured for 30 days after prior written notice; or (iv) the relocation of the Company's headquarters more than 25 miles away from San Diego, California.

Frederic Chereau

Mr. Chereau entered into an at-will employment agreement with us on December 20, 2013, which provided for an initial base salary of $360,000, subject to periodic review and adjustments as determined by the Company in its sole discretion. Pursuant to the terms of his employment agreement, Mr. Chereau is considered annually for a bonus target of up to 50% of his then-current base salary, as determined by our board of directors based on corporate achievements of goals and achievement of Mr. Chereau's individual goals. Pursuant to the terms of his employment agreement, Mr. Chereau was issued an option to purchase 249,907 shares of the Company's common stock on March 5, 2014. In connection with commencement of his employment, we granted Mr. Chereau a relocation assistance payment of $45,000 and reimbursed Mr. Chereau $36,000 for temporary housing.

David M. Weiner, M.D.

Dr. Weiner entered into an at-will employment agreement with us on February 20, 2014, which provided for an initial base salary of $335,000, subject to periodic review and adjustments as determined by the Company in its sole discretion. Pursuant to the terms of his employment agreement, Dr. Weiner is considered annually for a bonus target 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. Weiner's individual goals. Pursuant to the terms of his employment agreement, Dr. Weiner was issued an option to purchase 120,922 shares of the Company's common stock on July 10, 2014. In connection with commencement of his employment, we granted Dr. Weiner a relocation assistance payment of $50,000.

Outstanding Equity Awards at Fiscal Year-End

The following table summarizes, for each of the named executive officers, the number of outstanding equity awards held by each of our named executive officers as of December 31, 2014.

	Option Awards				Stock Awards	
	Number of Securities underlying Unexercised Options (#) Exercisable	Number of Securities underlying Unexercised Options (#) Unexercisable	Option Exercise Price ($)	Option Expiration Date	Number of Shares that Have Not Vested (#)	Market Value of Shares that Have Not Vested ($)(1)
John D. Mendlein, Ph.D	49,916	1,063(2)	0.72	3/16/2021	—	—
	26,392	15,836(3)	0.72	3/16/2021	—	—
	57,446	80,425(4)	0.88	9/13/2022	—	—
	33,115	86,099(5)	4.06	6/28/2023	—	—
	3,841	21,303(6)	4.06	3/5/2024	—	—
	—	—	—	—	24,247(7)	285,448
Frederic Chereau.	—	249,907(8)	4.06	3/5/2024	—	—
David M. Weiner, M.D	—	120,922(9)	4.06	7/10/2024	—	—

(1) There was no public market for our common stock as of December 31, 2014. The fair value of our common stock as of December 31, 2014 was $11.77 per share.
(2) Option vests with respect to 2.08% of the shares on each monthly anniversary of January 1, 2011.
(3) Option vests with respect to 1.39% of the shares on each monthly anniversary of March 16, 2011.
(4) Option vests with respect to 1.39% of the shares on each monthly anniversary of June 1, 2012.
(5) Option vests with respect to 1.39% of the shares on each monthly anniversary of April 19, 2013.
(6) Option vests with respect to 1.39% of the shares on each monthly anniversary of January 1, 2014.
(7) Represents shares subject to our repurchase right, which will lapse upon the completion of this offering.
(8) Option vests with respect to 1.39% of the shares on each monthly anniversary of January 9, 2014.
(9) Option vests with respect to 1.39% of the shares on each monthly anniversary of March 17, 2014

Director Compensation

The following table provides certain information concerning compensation earned by the directors who were not named executive officers during the year ended December 31, 2014.

Name	Fees Earned or Paid in Cash ($)	Option Awards ($)(1)(2)	Total ($)
James C. Blair, Ph.D.	13,750	150,397	164,147
John K. Clarke	11,250	150,397	161,647
Kathryn E. Falberg	22,500	150,397	172,897
Amir H. Nashat, Sc.D.	11,250	150,397	161,647
Edward Penhoet, Ph.D.(3)	10,000	150,397	160,397
Paul Schimmel, Ph.D.	11,250	150,397	161,647

(1) The amounts reported reflect the aggregate grant date fair value computed in accordance with ASC 718.
(2) Represents an option to purchase 12,572 shares of common stock at an exercise price of $4.06 per share granted to each of our non-employee directors in July 2014. The shares of common stock underlying each such option vest in 36 equal monthly installments over three years from June 1, 2014 through June 1, 2017. In November 2014, each of the options was amended to allow for the early exercise of the options, subject to our right of repurchase with respect to any unvested shares.
(3) Dr. Penhoet resigned from the board of directors as of April 2, 2015.

Our Chief Executive Officer received no compensation for his services as a director. Pursuant to our board of directors compensation plan, effective as of June 1, 2014, each non-employee director is paid a retainer fee of $20,000 per year, and each committee member is paid $2,500 per year. Committee chairs are paid $7,500 per year, with the exception of the audit committee chair, who is paid $25,000 per year. In addition, each director was eligible under this plan to receive an initial option grant of 12,572 shares and an annual option grant of 4,400 shares.

In April 2015, our board of directors adopted a non-employee director compensation policy, to be effective as of the completion of this offering, 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. Under this policy, all non-employee directors will be paid cash compensation as set forth below, prorated based on days of service during a calendar year:

Board of Directors	Annual Retainer
All non-employee members	$35,000
Additional retainer for Chairperson	$35,000
Audit Committee:	
Chairperson	$25,000
Non-Chairperson members	$ 5,000
Compensation Committee:	
Chairperson	$10,000
Non-Chairperson members	$ 5,000
Nominating and Corporate Governance Committee:	
Chairperson	$ 7,500
Non-Chairperson members	$ 3,500

In addition, under the policy, each new non-employee director who is initially appointed or elected to our board of directors after effectiveness of the policy will receive an option grant to purchase up to 12,572 shares of common stock, which will vest in equal monthly installments over a period of three years following the grant date, subject to the director's continued service on our board of directors. In addition, on the date of each annual

meeting of our stockholders, each continuing non-employee director will be eligible to receive an annual option grant to purchase 6,286 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. Our non-employee directors may also be granted such additional stock options in such amounts and on such dates as our board of directors may recommend. All of the foregoing options will be granted at fair market value on the date of grant and will be exercisable (to the extend vested) for up to one year following cessation of the director's service on our board of directors, so long as the director was not removed for cause.

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

Compensation Risk Assessment

We believe that although a portion of the compensation provided to our executive officers and other employees is performance-based, our executive compensation program does not encourage excessive or unnecessary risk taking. This is primarily due to the fact that our compensation programs are designed to encourage our executive officers and other employees to remain focused on both short-term and long-term strategic goals, in particular in connection with our pay-for-performance compensation philosophy. As a result, we do not believe that our compensation programs are reasonably likely to have a material adverse effect on our company.

Equity Compensation Plans

2014 Stock Plan

Our 2014 Stock Plan, or the 2014 Plan, was originally adopted by our board of directors and our stockholders in 2007, and was subsequently amended and restated in 2014. As of April 1, 2015, we have reserved an aggregate of 3,480,079 shares of our common stock for the issuance of options and other equity awards under the 2014 Plan. This number is subject to adjustment in the event of a consolidation, stock split, stock dividend or other change in our capitalization. Our board of directors has determined not to grant any further awards under our 2014 Plan. The shares we issue under the 2014 Plan are authorized but unissued shares or shares we reacquire. Prior to the effectiveness of the registration statement of which this prospectus forms a part, the shares of common stock underlying any awards that were forfeited, canceled, reacquired by us prior to vesting, satisfied without the issuance of stock or otherwise terminated (other than by exercise) under the 2014 Plan were added back to the shares of common stock available for issuance under the 2014 Plan. Following the effectiveness of the registration statement of which this prospectus forms a part, such reacquired shares will be added to the shares of common stock available for issuance under the 2015 Plan.

The 2014 Plan is administered by our compensation committee. Our board of directors and our compensation committee have the authority to select the individuals to whom awards will be granted, to make any combination of awards to participants, to accelerate the exercisability or vesting of any award, to provide substitute awards and to determine the specific terms and conditions of each award.

The 2014 Plan permits us to make grants of incentive stock options and non-qualified stock options, restricted stock awards and restricted stock unit awards to our employees, directors and consultants.

The 2014 Plan permits the granting of (1) options to purchase common stock intended to qualify as incentive stock options under Section 422 of the Internal Revenue Code, or the Code, and (2) options that do not so qualify. The option exercise price of each option is determined by our board or directors or our compensation committee but may not be less than 100% of the fair market value of our common stock on the date of grant. In the case of an incentive stock option granted to a participant who, at the time of grant of such option, owns stock representing more than 10% of the voting power of all classes of stock of the Company, then the exercise price may not be less than 110% of the fair market value of our common stock on the date of grant. The term of each option will be fixed by our board of directors or our compensation committee and may not exceed ten years from the date of grant.

The 2014 Plan provides that upon the occurrence of a change in control event, awards may be assumed, substituted for new awards of a successor entity, or otherwise continued or terminated at the effective time of such sale event. In the event any award is not assumed, substituted or otherwise continued in connection with a change in control event, such award will be subject to accelerated vesting. We may make or provide for cash payment to holders of options equal to the difference between the per share cash consideration in the sale event and the exercise price to the holders of vested and exercisable options. We may make or provide for cash payment to holders of restricted stock and restricted stock unit awards in an amount equal to the product of the per share cash consideration and the number of shares subject to each such award. In 2014, we amended certain outstanding option agreements under the 2014 Plan to provide for "double trigger" acceleration upon certain termination events which occur after a change in control event. Additionally, future stock options granted to our Chief Executive Officer and other executive officers as designated by our Chief Executive Officer will also be subject to "double trigger" acceleration unless otherwise determined by our board of directors.

Our board of directors may amend, suspend or terminate the 2014 Plan at any time, subject to stockholder approval where such approval is required by applicable law. Our board of directors may also amend, modify or terminate any outstanding award, provided that no amendment to an award may materially impair any of the rights of a participant under any awards previously granted without his or her written consent.

2015 Stock Option and Incentive Plan

In April 2015, our board of directors adopted, and our stockholders approved, our 2015 Stock Option and Incentive Plan, or the 2015 Plan. Our 2015 Plan became effective upon the effectiveness of the registration statement of which this prospectus forms a part and is not expected to be utilized until after the completion of this offering, except with respect to the grant of options to purchase an aggregate of 377,158 shares of common stock approved by our board of directors on April 17, 2015, which became effective immediately following the effectiveness of the registration statement of which this prospectus forms a part. Our 2015 Plan will provide for the grant of incentive stock options, within the meaning of Section 422 of the Code, to our employees and any of our parent and subsidiary corporations' employees, and for the grant of nonstatutory stock options, restricted stock, restricted stock units, stock appreciation rights, performance units and performance shares to our employees, directors and consultants, and our parent and subsidiary corporations' employees and consultants.

We have initially reserved 1,574,566 shares of our common stock, or the Initial Limit, for the issuance of awards under the 2015 Plan. The 2015 Plan provides that the number of shares reserved and available for issuance under the plan will automatically increase each January 1, from January 1, 2016 until January 1, 2019, by the lesser of (i) 1,840,000 shares of common stock, (ii) 4% of the outstanding number of shares of our common stock on the immediately preceding December 31, and (iii) an amount as determined by our compensation committee of our board of directors, or the Annual Increase. This number is subject to adjustment in the event of a stock split, stock dividend or other change in our capitalization.

The shares we issue under the 2015 Plan will be authorized but unissued shares or shares that we reacquire. The shares of common stock underlying any awards that are forfeited, cancelled, reacquired by us prior to vesting, satisfied without any issuance of stock, or are otherwise terminated (other than by exercise) under the 2015 Plan and 2014 Plan will be added back to the shares of common stock available for issuance under the 2015 Plan.

Stock options and stock appreciation rights with respect to no more than 1,574,566 shares of stock may be granted to any one individual in any one calendar year and the maximum "performance-based award" payable to any one individual under the 2015 Plan is 1,574,566 shares of stock or $2,000,000 in the case of cash-based awards. The maximum aggregate number of shares that may be issued in the form of incentive stock options shall not exceed the Initial Limit cumulatively increased on January 1, 2016 and on each January 1 thereafter until January 1, 2019 by the lesser of the Annual Increase for such year or 1,574,566 shares of common stock.

The 2015 Plan will be administered by our compensation committee. Our compensation committee has full power to select, from among the individuals eligible for awards, the individuals to whom awards will be granted, to make any combination of awards to participants, and to determine the specific terms and conditions of each award, subject to the provisions of the 2015 Plan. Persons eligible to participate in the 2015 Plan will be those full or part-time officers, employees, non-employee directors and other key persons (including consultants) as selected from time to time by our compensation committee in its discretion.

The 2015 Plan permits the granting of both options to purchase common stock intended to qualify as incentive stock options under Section 422 of the Code and options that do not so qualify. The option exercise price of each option will be determined by our compensation committee but may not be less than 100% of the fair market value of our common stock on the date of grant. The term of each option will be fixed by our compensation committee and may not exceed ten years from the date of grant. Our compensation committee will determine at what time or times each option may be exercised.

Our compensation committee may award stock appreciation rights subject to such conditions and restrictions as we may determine. Stock appreciation rights entitle the recipient to shares of common stock, equal to the value of the appreciation in our stock price over the exercise price. The exercise price of each stock appreciation right may not be less than 100% of the fair market value of our common stock on the date of grant.

Our compensation committee may award shares of restricted common stock and restricted stock units to participants subject to such conditions and restrictions as it may determine. These conditions and restrictions may include the achievement of certain performance goals and continued employment with us through a specified vesting period. Our compensation committee may also grant shares of common stock that are free from any restrictions under the 2015 Plan. Unrestricted stock may be granted to participants in recognition of past services or other valid consideration and may be issued in lieu of cash compensation due to such participant.

Our compensation committee may grant performance share awards to participants that entitle the recipient to receive shares of common stock upon the achievement of certain performance goals and such other conditions as our compensation committee shall determine.

Our compensation committee may grant cash bonuses under the 2015 Plan to participants, subject to the achievement of certain performance goals.

Our compensation committee may grant awards of restricted stock, restricted stock units, performance shares or cash-based awards under the 2015 Plan that are intended to qualify as “performance-based compensation” under Section 162(m) of the Code. Those awards would only vest or become payable upon the attainment of performance goals that are established by our compensation committee and related to one or more performance criteria. The performance criteria that would be used with respect to any such awards 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 and 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, stockholder returns, return on sales, gross or net profit levels, productivity, expense, margins, operating efficiency, customer satisfaction, working capital, earnings (loss) per share of stock, sales or market shares and number of customers, any of which may be measured either in absolute terms or as compared to any incremental increase or as compared to results of a peer group.

The 2015 Plan provides that in the case of, and subject to, the consummation of a “sale event” as defined in the 2015 Plan, all outstanding awards may be assumed, substituted or otherwise continued by the successor entity. To the extent that the successor entity does not assume, substitute or otherwise continue such awards, then upon the effectiveness of the sale event, all stock options and stock appreciation rights will automatically

terminate. In the event of such termination, individuals holding options and stock appreciation rights will be permitted to exercise such options and stock appreciation rights prior to the sale event. In addition, in connection with a sale event, we may make or provide for a cash payment to participants holding options and stock appreciation rights equal to the difference between the per share cash consideration payable to stockholders in the sale event and the exercise price of the options or stock appreciation rights.

Our board of directors may amend or discontinue the 2015 Plan and our compensation committee may amend or cancel outstanding awards for purposes of satisfying changes in law or any other lawful purpose, but no such action may adversely affect rights under an award without the holder's consent. Certain amendments to the 2015 Plan require the approval of our stockholders.

No awards may be granted under the 2015 Plan after the date that is ten years from the effective date of the 2015 Plan. No awards under the 2015 Plan have been made prior to the date hereof.

2015 Employee Stock Purchase Plan

In April 2015, our board of directors adopted, and our stockholders approved, our 2015 Employee Stock Purchase Plan, or the 2015 ESPP. The 2015 ESPP became effective upon the effectiveness of the registration statement of which this prospectus forms a part.

The 2015 ESPP authorizes the initial issuance of up to a total of 227,623 shares of our common stock to participating employees. The 2015 ESPP provides that the number of shares reserved and available for purchase under the plan will automatically increase each January 1, from January 1, 2016 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. This number is subject to adjustment in the event of a stock split, stock dividend or other change in our capitalization.

All employees who have been employed by us or our designated subsidiaries for at least six months and whose customary employment is for more than 20 hours a week are eligible to participate in the 2015 ESPP. Any employee who owns, or would own upon such purchase under the 2015 ESPP, 5% or more of the voting power or value of our stock is not eligible to purchase shares under our the 2015 ESPP.

We may make one or more offerings to our employees to purchase stock under the 2015 ESPP. Unless otherwise determined by the administrator of the 2015 ESPP, each offering will begin on the first business day occurring on or after each January 1st and July 1st and will end on the last business day occurring on or before the following June 30th and December 31st, respectively, each referred to as offering periods. The administrator may designate different offering periods in its discretion but no offering shall exceed 12 months in duration or overlap with another offering.

Each employee who is a participant in the 2015 ESPP may purchase shares by authorizing payroll deductions at a minimum of 1% and up to 15% of his or her eligible compensation for each pay period. Unless the participating employee has previously withdrawn from the offering, his or her accumulated payroll deductions will be used to purchase common stock on the last business day of the offering period at a price equal to 85% of the fair market value of the common stock on either the first or the last day of the offering period, whichever is lower, provided that no more than 2,500 shares of common stock or such other lesser maximum number established by the plan administrator may be purchased by any one employee during each offering period. Under applicable tax rules, an employee may purchase no more than $25,000 worth of common stock, valued at the start of the purchase period, under the 2015 ESPP in any calendar year.

The accumulated payroll deductions of any employee who is not a participant on the last day of an offering period will be refunded. An employee's rights under the 2015 ESPP terminate upon voluntary withdrawal from the plan or when the employee ceases employment for any reason.

The 2015 ESPP may be terminated or amended by our board of directors at any time. Amendments that increase the number of shares of our common stock authorized under the 2015 ESPP and certain other amendments require the approval of our stockholders.

401(k) Plan and Other Benefits

We maintain a tax-qualified retirement plan, or the 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. In April 2015, our board of directors approved a policy under which, beginning on June 1, 2015, we will 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, the premiums for health, life and disability insurance.

Pension Benefits, Non-Qualified Contribution Plans and other Non-Qualified Defined Compensation Plans

We do not provide a pension plan or non-qualified defined contribution plans for any of our employees, and none of our named executive officers participated in a non-qualified defined compensation plan during the fiscal year ended December 31, 2014.

CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

Other than the compensation agreements and other arrangements described under "Executive and Director Compensation" in this prospectus and the transactions described below, since January 1, 2012, 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 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.

Private Placements of Securities

2013 Convertible Note Financing

In March 2013, we issued convertible promissory notes, or the 2013 Notes, in an aggregate principal amount of $10,000,000 to certain existing stockholders. A portion of the principal amount of the 2013 Notes converted into Series D redeemable convertible preferred stock in April 2013. The remainder of the principal amount of the 2013 Notes was repaid through cancellation of indebtedness pursuant to the Securities Purchase Agreements entered into with the Affiliates (as defined in "Management's Discussion and Analysis of Financial Condition and Results of Operations—Financial Operations Overview"). The following table summarizes participation in our convertible note financing by related persons:

Stockholder	Principal Amount of Notes Purchased	Amount of Notes Converted into Series D Redeemable Convertible Preferred Stock
Entities affiliated with Paul Schimmel, Ph.D.	$ 697,574.30	$ 665,266.10
John D. Mendlein, Ph.D.	$ 31,888.71	$ 30,413.76
CHP II, L.P.	$ 2,331,981.85	$ 2,223,969.73
Entities affiliated with Polaris Venture Management Co. V, LLC	$ 2,300,891.40	$ 2,194,322.28
Entities affiliated with Alta Partners Management VIII, LLC	$ 2,300,891.40	$ 2,194,319.73
Entities affiliated with Domain Partners VIII, L.P.	$ 2,291,930.35	$ 2,185,774.25

Series D Redeemable Convertible Preferred Stock Financing

In April 2013 and May 2013, we sold an aggregate of 18,275,830 shares of our Series D redeemable convertible preferred stock at a purchase price of $2.529 per share for an aggregate purchase price of $46,219,574.22, $9,536,813.24 of which was paid in cancellation of indebtedness under the 2013 Notes. The Affiliates also sold an aggregate of 19,364,416 of their Series D redeemable convertible preferred stock at an average purchase price of $0.022, for an aggregate purchase price of $2,575,467.33. We and the Affiliates entered into an Amended and Restated Affiliate Agreement under which each of our stockholders was entitled to receive stock in each Affiliate in proportion to the amount of our stock held by such stockholder, subject to certain adjustments. Under the Series D redeemable convertible preferred stock Securities Purchase Agreement, each investor in the our Series D redeemable convertible preferred stock was required to enter into a Securities Purchase Agreement with each of the Affiliates for the sale and issuance of Series D Preferred Stock of such Affiliates. The following table summarizes purchases of our Series D redeemable convertible preferred stock by related persons:

Stockholder	Shares of our Series D Redeemable Convertible Preferred Stock	Total Purchase Price (1)
Entities affiliated with Paul Schimmel, Ph.D.	263,055	$ 700,252.41
John D. Mendlein, Ph.D.	21,122	$ 56,226.71
CHP II, L.P.	1,536,787	$ 4,090,926.99
Entities affiliated with Polaris Venture Management Co. V, LLC	1,524,018	$ 4,056,935.92
Entities affiliated with Alta Partners Management VIII, LLC	1,126,866	$ 2,999,717.29
Entities affiliated with Domain Partners VIII, L.P.	1,518,083	$ 4,041,136.95
Entities affiliated with FMR LLC	12,002,254	$ 31,950,000.15

(1) The table reflects the total purchase price of $2.662 per share. The Company received $2.529 per share, with the Affiliates receiving the remaining $0.133 per share.

Series E Redeemable Convertible Preferred Stock Financing

In March 2015, we sold an aggregate of 68,166,894 shares of our Series E redeemable convertible preferred stock at a purchase price of $1.119 per share for an aggregate purchase price of $76,278,754.55. Upon completion of this offering, each share of Series E redeemable convertible preferred stock is convertible into shares of our common stock at a rate of one share of preferred stock into 0.10329 shares of common stock. The following table summarizes purchases of our Series E redeemable convertible preferred stock by related persons:

Stockholder	Shares of our Series E Redeemable Convertible Preferred Stock	Total Purchase Price
John K. Clarke	893,655	$ 999,999.95
Paul Schimmel, Ph.D. and affiliated entities	446,827	$ 499,999.42
Entities affiliated with Polaris Venture Management Co. V, LLC	893,653	$ 999,997.73
Entities affiliated with Alta Partners Management Co. V, LLC	893,655	$ 999,999.95
Entities affiliated with Domain Partners VIII, L.P.	893,654	$ 999,998.83
Entities affiliated with FMR LLC	8,113,286	$ 9,078,767.04
Sofinnova Venture Partners IX, L.P.	14,968,722	$ 16,749,999.92
Entities affiliated with Baker Brothers Life Sciences, L.P.	14,968,722	$ 16,749,999.92

Loan to Chief Executive Officer and Executive Chairman

In July 2010, we loaned $69,432.30 in principal amount to John D. Mendlein, Ph.D., our Chief Executive Officer and Executive Chairman, in connection with Dr. Mendlein's purchase of restricted shares of our common

stock. The loan was evidenced by a Secured Promissory Note and Pledge Agreement and bore interest at an annual rate of 5%. The loan was secured by 96,989 shares of our common stock. In January 2015, Dr. Mendlein repaid the full outstanding principal and accrued interest under the loan, totaling $85,021.27 in the aggregate.

Payments and Stock Issuance to The Scripps Research Institute

We provide funding to The Scripps Research Institute, or TSRI, under an amended and restated research funding and option agreement. See "Business" for more information about this agreement. Since January 1, 2012, we have paid $2,229,720.50 to TSRI under the agreement. Pursuant to the terms of the amended and restated research funding and option agreement, in March 2015, we issued 119,840 shares of our common stock to TSRI in consideration of certain rights granted by TSRI to us. Paul Schimmel, Ph.D., one of our directors, is a faculty member at TSRI and such payments fund a portion of his research activities conducted at TSRI.

Charitable Donations to National Foundation for Cancer Research

Since January 1, 2012, we have provided charitable donations to the National Foundation for Cancer Research, or NFCR, in the aggregate amount of $1,172,000. We have requested that the donations be restricted to a laboratory that performs basic research on the role of aminoacyl tRNA synthetase fragments and splice variants in cancer biology and therapeutics. The NFCR in its discretion selected Dr. Schimmel's laboratory at TSRI as the laboratory to receive these funds.

Executive Officer and Director Compensation

Employment Agreements

We have entered into offer letters or employment related agreements with each of John D. Mendlein, Ph.D., Frederic Chereau, David M. Weiner, M.D. and certain of our executive officers. For more information regarding these arrangements, see "Executive and Director Compensation—Employment Arrangements with Our Named Executive Officers."

Consulting Agreement

In January 2012, we entered into a Consulting Agreement with Holly D. Chrzanowski, our current Vice President, Enterprise Talent and Organization. Under this agreement, we paid Ms. Chrzanowski an aggregate total of $151,322.50 in the fiscal year ending December 31, 2012 and an aggregate total of $101,197.50 in the fiscal year ending December 31, 2013. We hired Ms. Chrzanowski as our Vice President, Enterprise Talent and Organization in April 2013.

Restricted Stock and Stock Option Awards

For information regarding restricted stock and stock option awards granted to our named executive officers and directors, see "Executive and Director Compensation."

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.

Registration and Voting Rights Agreement

We and certain holders of our capital stock have entered into a registration and voting rights agreement pursuant to which these stockholders will have, among other things, registration rights under the Securities Act of 1933, or the Securities Act, with respect to common stock that they will hold following this offering. In addition, pursuant to this agreement, certain holders of our capital stock who previously held our Series E redeemable convertible preferred stock prior to the completion of this offering may designate one individual as a nominee to serve on our board of directors and certain of such holders have a right of first offer with respect to any proposed sales of our common stock or securities convertible into or exercisable or exchangeable for our common stock, subject to certain conditions. See "Description of Capital Stock—Registration and Voting Rights" for a further description of the terms of this agreement.

Participation in this Offering

Certain of our existing stockholders, including a stockholder affiliated with one of our directors, have indicated an interest in purchasing, and have agreed to purchase, an aggregate of 1,070,000 shares of our common stock in this offering at the initial public offering price as follows:

Beneficial Owner	Shares to be Purchased in Offering
Entities affiliated with Baker Brothers Life Sciences, L.P.	750,000
Sofinnova Venture Partners IX, L.P.	320,000

The information above does not reflect any potential purchases in this offering by other existing stockholders.

The underwriting discount for the shares sold to these investors in the offering will be the same as the underwriting discount for the shares sold to the public.

Policies for Approval of Related Party Transactions

Our board of directors reviews and approves transactions with directors, officers and holders of five percent or more of our voting securities and their affiliates, each a related party. Prior to this offering, the material facts as to the related party's relationship or interest in the transaction are disclosed to our board of directors prior to their consideration of such transaction, and the transaction is not considered approved by our board of directors unless a majority of the directors who are not interested in the transaction approve the transaction. Further, when stockholders are entitled to vote on a transaction with a related party, the material facts of the related party's relationship or interest in the transaction are disclosed to the stockholders, who must approve the transaction in good faith.

In connection with this offering, we have adopted a written related party transactions policy that such transactions must be approved by our audit committee or another independent body of our board of directors.

PRINCIPAL STOCKHOLDERS

The following table sets forth certain information known to us regarding beneficial ownership of our capital stock as of March 31, 2015, as adjusted to reflect the sale of common stock offered by us in this offering, for:

- each person or group of affiliated persons known by us to be the beneficial owner of more than five percent of our capital stock;
- our named executive officers;
- each of our other directors; and
- all executive officers and directors as a group.

To the extent that the underwriters sell more than 5,360,000 shares in this offering, the underwriters have the option to purchase up to an additional 804,000 shares at the initial public offering price less the underwriting discount.

Certain of our existing stockholders, including a stockholder affiliated with one of our directors, have indicated an interest in purchasing, and have agreed to purchase, an aggregate of 1,070,000 shares of our common stock in this offering at the initial public offering price. The underwriting discount for the shares sold to these investors in the offering will be the same as the underwriting discount for the shares sold to the public. The information set forth below does not reflect any purchases in this offering by these investors or any other existing stockholders.

Beneficial ownership is determined in accordance with the rules of the Securities and Exchange Commission and generally includes voting or investment power with respect to securities. Except as noted by footnote, and subject to community property laws where applicable, we believe based on the information provided to us that the persons and entities named in the table below have sole voting and investment power with respect to all common stock shown as beneficially owned by them.

The percentage of beneficial ownership prior to this offering in the table below is based on 17,309,590 shares of common stock deemed to be outstanding as of March 31, 2015, assuming conversion of all outstanding shares of redeemable convertible preferred stock into shares of our common stock at a rate of one share of redeemable convertible preferred stock into 0.12572 shares of common stock, except for our Series E redeemable convertible preferred stock, for which the conversion rate is one share of Series E redeemable convertible preferred stock into 0.10329 shares of common stock, and the percentage of beneficial ownership after this offering in the table below is based on 22,669,590 shares of common stock assumed to be outstanding after the closing of the offering. The information in the table below assumes no exercise of the underwriters' option to purchase additional shares. Options to purchase shares of common stock that are exercisable within 60 days of March 31, 2015 are deemed to be beneficially owned by the persons holding these options for the purpose of computing percentage ownership of that person, but are not treated as outstanding for the purpose of computing any other person's ownership percentage.

Name and Address of Beneficial Owner (1)	Number of Shares Beneficially Owned before Offering	Percentage of Shares Beneficially Owned before Offering	Number of Shares Beneficially Owned after Offering	Percentage of Shares Beneficially Owned after Offering
5% Stockholders:				
CHP II, L.P. (2)	1,758,158	10.16%	1,758,158	7.76%
Entities affiliated with Polaris Venture Management Co. V, LLC (3)	1,827,992	10.56%	1,827,992	8.06%
Entities affiliated with Alta Partners Management VIII, LLC (4)	1,778,064	10.27%	1,778,064	7.84%
Entities affiliated with Domain Partners VIII, L.P. (5)	1,821,234	10.52%	1,821,234	8.03%
Entities affiliated with FMR LLC (6)	2,346,954	13.56%	2,346,954	10.35%
Sofinnova Venture Partners IX, L.P. (7)	1,546,126	8.93%	1,546,126	6.82%
Entities affiliated with Baker Brothers Life Sciences, L.P. (8)	1,546,125	8.93%	1,546,125	6.82%
Executive Officers and Directors:				
John D. Mendlein, Ph.D. (9)	440,275	2.52%	440,275	1.93%
Frederic Chereau (10)	55,534	*	55,534	*
David M. Weiner, M.D. (11)	23,512	*	23,512	*
James C. Blair, Ph.D. (5)(12)	1,833,806	10.59%	1,833,806	8.08%
John K. Clarke (2)(13)	1,863,036	10.76%	1,863,036	8.21%
Srinivas Akkaraju, M.D., Ph.D.(7)	1,546,126	8.93%	1,546,126	6.82%
Kathryn E. Falberg (14)	12,572	*	12,572	*
Amir H. Nashat, Sc.D. (3)(15)	1,840,564	10.63%	1,840,564	8.11%
Paul Schimmel, Ph.D. (16)	689,920	3.98%	689,920	3.04%
Mark Goldberg, M.D. (17)	—	*	—	*
All executive officers and directors as a group (17 persons)(18)	8,471,759	47.67%	8,471,759	36.62%

* Represents beneficial ownership of less than one percent.

(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) Consists of an aggregate of 1,758,158 shares of common stock issuable upon conversion of: 2,400,000 shares of Series A redeemable convertible preferred stock, 3,600,000 shares of Series B redeemable convertible preferred stock, 4,320,173 shares of Series B-2 redeemable convertible preferred stock, 2,127,660 shares of Series C redeemable convertible preferred stock and 1,536,787 shares of Series D redeemable convertible preferred stock, all 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. One of our directors, 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. The mailing address of the beneficial owner is c/o Cardinal Partners, 230 Nassau Street, Princeton, NJ 08542.

(3) Consists of an aggregate of 1,827,992 shares of common stock issuable upon conversion of: (i) 3,473,763 shares of Series B redeemable convertible preferred stock, 4,168,683 shares of Series B-2 redeemable convertible preferred stock, 4,208,756 shares of Series C redeemable convertible preferred stock, 1,470,577 shares of Series D redeemable convertible preferred stock and 862,318 shares of Series E redeemable convertible preferred stock, which shares are convertible into 89,069 shares of common stock at a rate of one share of Series E redeemable convertible preferred stock into approximately 0.10329 of a share of common stock, all held by Polaris Venture Partners V, L.P. ("Polaris Ventures"), (ii) 67,704 shares of Series B redeemable convertible preferred stock, 81,248 shares of Series B-2 redeemable convertible preferred stock, 82,029 shares of Series C redeemable convertible preferred stock, 28,661 shares of Series D redeemable convertible preferred stock and 16,806 shares of Series E redeemable convertible preferred stock, which shares are convertible into 1,735 shares of common stock at a rate of one share of Series E

redeemable convertible preferred stock into approximately 0.10329 of a share of common stock, all held by Polaris Venture Partners Entrepreneurs' Fund V, L.P. ("Polaris Entrepreneurs' Fund"), (iii) 23,796 shares of Series B redeemable convertible preferred stock, 28,556 shares of Series B-2 redeemable convertible preferred stock, 28,831 shares of Series C redeemable convertible preferred stock, 10,074 shares of Series D redeemable convertible preferred stock and 5,906 shares of Series E redeemable convertible preferred stock, which shares are convertible into 610 shares of common stock at a rate of one share of Series E redeemable convertible preferred stock into approximately 0.10329 of a share of common stock, all held by Polaris Venture Partners Founders' Fund V, L.P. ("Polaris Founders' Fund") and (iv) 34,737 shares of Series B redeemable convertible preferred stock, 41,686 shares of Series B-2 redeemable convertible preferred stock, 42,087 shares of Series C redeemable convertible preferred stock, 14,706 shares of Series D redeemable convertible preferred stock and 8,623 shares of Series E redeemable convertible preferred stock, which shares are convertible into 890 shares of common stock at a rate of one share of Series E redeemable convertible preferred stock into approximately 0.10329 of a share of common stock, all held by Polaris Venture Partners Special Founders' Fund V, L.P. ("Polaris Special Founders' Fund"). Each of the funds has sole voting and investment power with respect to the shares held by such funds. The general partner of Polaris Ventures, Polaris Entrepreneurs' Fund, Polaris Founders' Fund and Polaris Special Founders' Fund is Polaris Venture Management Co. V, LLC ("Polaris Management"), and Polaris Management may be deemed to have sole voting and investment power over such shares. Director Amir H. Nashat is one of six members of Polaris Management. He has shared voting and investment power over such shares and may be deemed the indirect beneficial owner of such shares. The members of North Star Venture Management 2010 LLC are also members of Polaris Management, and as members of the general partner, they may be deemed to share voting and investment power over such shares. The mailing address of the beneficial owner is 1000 Winter Street, Suite 3350, Waltham, MA 02451.

(4) Consists of an aggregate of 1,778,064 shares of common stock issuable upon conversion of: 3,600,000 shares of Series B redeemable convertible preferred stock, 4,320,173 shares of Series B-2 redeemable convertible preferred stock, 4,361,703 shares of Series C redeemable convertible preferred stock, 1,126,866 shares of Series D redeemable convertible preferred stock and 893,655 shares of Series E redeemable convertible preferred stock, which shares are convertible into 92,306 shares of common stock at a rate of one share of Series E redeemable convertible preferred stock into approximately 0.10329 of a share of common stock, all held by Alta Partners VIII, L.P. ("Alta Partners"). Alta Partners Management VIII, LLC ("Alta Management") is the general partner of Alta Partners and as the general partner may be deemed to have beneficial ownership of the shares held by Alta Partners. Alta Managers disclaims beneficial ownership of all such shares in which they do not have an actual pecuniary interest. The managing directors of Alta Management are Daniel Janney, Farah Champsi and Guy Nohra, and as managing directors of the general partner, they may be deemed to share voting and investment power over such shares. The managing directors disclaim beneficial ownership of all shares held by Alta Management in which they do not have an actual pecuniary interest. The mailing address of the beneficial owner is One Embarcadero Center, 37th Floor, San Francisco, CA 94111.

(5) Consists of an aggregate of 1,821,234 shares of common stock issuable upon conversion of: (i) 12,143,933 shares of Series C redeemable convertible preferred stock, 1,506,901 shares of Series D redeemable convertible preferred stock and 887,073 shares of Series E redeemable convertible preferred stock, which shares are convertible into 91,626 shares of common stock at a rate of one share of Series E redeemable convertible preferred stock into approximately 0.10329 of a share of common stock, all held by Domain Partners VIII, L.P. ("Domain Partners") and (ii) 90,110 shares of Series C redeemable convertible preferred stock, 11,182 shares of Series D redeemable convertible preferred stock and 6,581 shares of Series E redeemable convertible preferred stock, which shares are convertible into 679 shares of common stock at a rate of one share of Series E redeemable convertible preferred stock into approximately 0.10329 of a share of common stock, all held by DP VIII Associates, L.P. ("Domain Associates"). One Palmer Square Associates VIII, L.L.C. ("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. One of our directors, 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. The mailing address of the beneficial owner is One Palmer Square, Suite 515, Princeton, New Jersey 08542.

(6) Consists of an aggregate of 2,346,954 shares of common stock issuable upon the conversion of: (i) 3,455,296 shares of Series D redeemable convertible preferred stock and 2,335,712 shares of Series E redeemable convertible preferred stock, which shares are convertible into 241,256 shares of common stock at a rate of one share of Series E redeemable convertible preferred stock into approximately 0.10329 of a share of common stock, all held by Fidelity Select Portfolios: Biotechnology Portfolio ("Fidelity Select"), (ii) 282,494 shares of Series D redeemable convertible preferred stock and 190,960 shares of Series E redeemable convertible preferred stock, which shares are convertible into 19,724 shares of common stock at a rate of one share of Series E redeemable convertible preferred stock into approximately 0.10329 of a share of common stock, all held by Fidelity Advisor Series VII: Fidelity Advisor Biotechnology Fund ("Fidelity Advisor Biotechnology"), (iii) 7,513,149 shares of Series D redeemable convertible preferred stock and 5,078,740 shares of Series E redeemable convertible preferred stock, which shares are convertible into 524,585 shares of common stock at a rate of one share of Series E redeemable convertible preferred stock into approximately 0.10329 of a share of common stock, all held by Fidelity Mt. Vernon Street Trust: Fidelity Growth Company Fund ("Fidelity Mt. Vernon Street"), (iv) 112,697 shares of Series D redeemable convertible preferred stock and 76,181 shares of Series E redeemable convertible preferred stock, which shares are convertible into 7,868 shares of common stock at a rate of one share of Series E redeemable convertible preferred stock into approximately 0.10329 of a share of common stock, all held by Variable Insurance Products Fund III: Growth Opportunities Portfolio ("Fidelity Variable Insurance") and (v) 638,618 shares of Series D redeemable convertible preferred stock and 431,693 shares of Series E redeemable convertible preferred stock, which shares are convertible into 44,589 shares of common stock at a rate of one share of Series E redeemable convertible preferred stock into approximately 0.10329 of a share of common stock, all held by Fidelity Advisor Series I: Fidelity Advisor Growth Opportunities Fund ("Fidelity Advisor Growth"). Fidelity Select, Fidelity Advisor Biotechnology, Fidelity Mt. Vernon Street, Fidelity Variable Insurance and Fidelity Advisor Growth are managed by direct or indirect subsidiaries of FMR LLC. Edward C. Johnson 3d is a Director and the Chairman of FMR LLC and Abigail P. Johnson is a Director, the Vice Chairman and the President of FMR LLC. Members of the family of Edward C. Johnson 3d, 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 Edward C. Johnson 3d nor Abigail P. Johnson has 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) Consists of 1,546,126 shares of common stock issuable upon the conversion of 14,968,722 shares of Series E redeemable convertible preferred stock, which shares are convertible into at a rate of one share of Series E redeemable convertible preferred stock into approximately 0.10329 of a share of common stock, held by Sofinnova Venture Partners IX, L.P. ("SVP IX"). Sofinnova Management IX, L.L.C. ("SM IX"), the general partner of SVP IX, may be deemed to have sole voting and dispositive power, and Dr. James I. Healy, Michael F. Powell, Ph.D., Dr. Srinivas Akkaraju and Dr. Anand Mehra, the managing members of SM IX, may be deemed to have shared voting and dispositive power, with respect to such shares. Such persons and entities disclaim beneficial ownership of the shares listed herein, except to the extent of any pecuniary interest therein. The address of SVP IX is c/o Sofinnova Ventures, Inc., 3000 Sand Hill Road, Bldg. 4, Suite 250, Menlo Park, California 94025.

(8) Consists of an aggregate of 1,546,125 shares of common stock issuable upon conversion of: (i) 13,953,918 shares of Series E redeemable convertible preferred stock, which shares are convertible into 1,441,306 shares of common stock at a rate of one share of Series E redeemable convertible preferred stock into approximately 0.10329 of a share of common stock, held by Baker Brothers Life Sciences, L.P. and (ii) 1,014,804 shares of Series E redeemable convertible preferred stock, which shares are convertible into 104,819 shares of common stock at a rate of one share of Series E redeemable convertible preferred stock into approximately 0.10329 of a share of common stock, held by 667, L.P. These entities are direct holders of Series E redeemable convertible preferred stock and are under the advisement of Baker Bros. Advisors LP. As advisor to the above entities, Baker Bros. Advisors LP has beneficial ownership over 14,968,722 shares in total.

(9) Consists of: (i) 221,916 shares of common stock, 24,247 of which are subject to our right of repurchase, which will lapse upon the completion of this offering, (ii) 21,399 shares of common stock issuable upon conversion of 170,218 shares of Series C redeemable convertible preferred stock, (iii) 2,655 shares of common stock issuable upon conversion of 21,122 shares of Series D redeemable convertible preferred stock and (iv) options to purchase an additional 194,304 shares of common stock that are exercisable within 60 days of March 31, 2015, held by Dr. Mendlein.

(10) Consists of options to purchase 55,534 shares of common stock that are exercisable within 60 days of March 31, 2015, held by Mr. Chereau.

(11) Consists of options to purchase 23,512 shares of common stock that are exercisable within 60 days of March 31, 2015, held by Dr. Weiner.

(12) Consists of options to purchase 12,572 shares of common stock that are exercisable within 60 days of March 31, 2015, 8,731 shares of which would be subject to our right of repurchase, held by Dr. Blair.

(13) Consists of an aggregate of 104,878 shares of common stock issuable upon conversion of: (i) 893,655 shares of Series E redeemable convertible preferred stock, which shares are convertible into 92,306 shares of common stock at a rate of one share of Series E redeemable convertible preferred stock into approximately 0.10329 of a share of common stock, and (ii) options to purchase 12,572 shares of common stock that are exercisable within 60 days of March 31, 2015, 8,731 shares of which would be subject to our right of repurchase, held by Mr. Clarke.

(14) Consists of options to purchase 12,572 shares of common stock that are exercisable within 60 days of March 31, 2015, 8,731 shares of which would be subject to our right of repurchase, held by Ms. Falberg.

(15) Consists of options to purchase 12,572 shares of common stock that are exercisable within 60 days of March 31, 2015, 8,731 shares of which would be subject to our right of repurchase, held by Dr. Nashat.

(16) Consists of an aggregate of 689,920 shares of common stock issuable upon conversion of: (i) 248,024 shares of Series D redeemable convertible preferred stock held by the Paul R. Schimmel Prototype PSP, (ii) 1,034,000 shares of common stock, 525,000 shares of Series A redeemable convertible preferred stock, 1,200,000 shares of Series B redeemable convertible preferred stock, 1,440,058 shares of Series B-2 redeemable convertible preferred stock, 558,508 shares of Series C redeemable convertible preferred stock, 15,031 shares of Series D redeemable convertible preferred stock and 446,827 shares of Series E redeemable convertible preferred stock, which shares are convertible into 46,152 shares of common stock at a rate of one share of Series E redeemable convertible preferred stock into approximately 0.10329 of a share of common stock, all held by the Schimmel Revocable Trust U/A Dtd 9/6/2000 and (iii) options to purchase an additional 12,572 shares of common stock that are exercisable within 60 days of March 31, 2015, 8,731 shares of which would be subject to our right of repurchase, held by Dr. Schimmel.

(17) Dr. Goldberg joined our board of directors on April 25, 2015.

(18) Includes the number of shares beneficially owned by the named executive officers and directors listed in the above table, as well as (i) 40,653 shares of common stock and options to purchase 28,458 shares of common stock that are exercisable within 60 days of March 31, 2015, held by Dr. Ashlock, (ii) options to purchase 5,327 shares of common stock that are exercisable within 60 days of March 31, 2015, held by Dr. Ramsdell, (iii) 279 shares of common stock and options to purchase 17,701 shares of common stock that are exercisable within 60 days of March 31, 2015, held by Ms. Blackburn, (iv) options to purchase 52,205 shares of common stock that are exercisable within 60 days of March 31, 2015, held by Dr. Cubitt, and (v) options to purchase 21,791 shares of common stock that are exercisable within 60 days of March 31, 2015, held by Ms. Chrzanowski.

DESCRIPTION OF CAPITAL STOCK

The following descriptions are summaries of the material terms of our amended and restated certificate of incorporation and amended and restated bylaws, which will be effective upon completion of this offering. The descriptions of the common stock and preferred stock give effect to changes to our capital structure that will occur immediately prior to the completion of this offering. We refer in this section to our amended and restated certificate of incorporation as our certificate of incorporation, and we refer to our amended and restated bylaws as our bylaws.

General

Upon completion of this offering and after giving effect to the conversion into common stock and retirement of all outstanding shares of our redeemable convertible preferred stock, our authorized capital stock will consist of 150,000,000 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 will be designated Series B redeemable convertible preferred stock, 15,957 shares will be designated Series C redeemable convertible preferred stock, 2,197,499 shares will be designated Series D redeemable convertible preferred stock and 5,000,000 shares will be undesignated preferred stock. In April 2015, our board of directors approved the retirement, upon the conversion of all shares of designated preferred stock into common stock in connection with the closing of this offering, of all such shares of designated preferred stock such that they will be cancelled and will not be subject to future reissuance. In addition, upon the conversion of all shares of our outstanding designated preferred stock into common stock in connection with the closing of this offering, no authorized but unissued shares of such designated preferred stock may thereafter be issued.

As of March 31, 2015, 17,309,590 shares of our common stock were deemed to be outstanding and held by 102 stockholders of record. This amount assumes the conversion of all outstanding shares of our redeemable convertible preferred stock into common stock, which will occur immediately prior to the closing of this offering. In addition, as of March 31, 2015, we had outstanding options to purchase 1,799,392 shares of our common stock under our 2014 Plan, at a weighted average exercise price of $5.33 per share.

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. The shares to be issued by us in this offering will be, when issued and paid for, validly issued, fully paid and non-assessable.

Preferred Stock

Immediately prior to the completion of this offering, all outstanding shares of our redeemable convertible preferred stock will be converted into shares of our common stock, and all such shares of redeemable convertible preferred stock will be retired such that they will be cancelled and no longer subject to reissuance. Immediately prior to the completion of this offering, our amended and restated certificate of incorporation will be restated to reflect the conversion and retirement of such shares of redeemable convertible preferred stock. Upon the consummation of this offering and after giving effect to the conversion and retirement of all outstanding shares

of our redeemable convertible preferred stock, we will have 2,285,456 shares of redeemable convertible preferred stock designated but not available for future issuance, and our board of directors will have the authority, without further action by our stockholders, to issue up to 5,000,000 shares of preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges could include 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 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. Immediately after consummation of this offering, no shares of preferred stock will be outstanding, and we have no present plan to issue any shares of preferred stock.

Warrants

As of March 31, 2015, we had outstanding warrants to purchase 72,000 shares of Series B redeemable convertible preferred stock, 15,957 shares of Series C redeemable convertible preferred stock and 118,624 shares of Series D redeemable convertible preferred stock, which are exercisable for an aggregate of 25,970 shares of common stock upon completion of this offering.

In September 2007, in connection with a loan and security agreement entered into with Comerica Bank, or Comerica, we issued to Comerica a warrant to purchase 72,000 shares of our Series B redeemable convertible preferred stock. The warrant contains provisions for the adjustment of the exercise price and the number of shares issuable upon the exercise of the warrant in the event of certain stock dividends, stock splits, recapitalizations, reclassifications, exchanges, substitutions, consolidations, combinations and other similar events. In addition, the number of shares of common stock issuable upon conversion of the shares of Series B redeemable convertible preferred stock underlying the warrant are subject to adjustment for certain dilutive issuances pursuant to our certificate of incorporation as in effect prior to the completion of this offering. The provision for adjustment upon dilutive issuances is an element of the preferred stock into which the warrant is currently exercisable. Upon completion of this offering, the warrants will become exercisable for 9,051 shares of common stock and will no longer be subject to adjustment for dilutive issuances because our common stock is not subject to any provision for adjustment for dilutive issuances. The warrant expires on September 18, 2017, unless the Company is acquired prior to that time in a transaction in which the consideration paid by the acquirer is comprised solely of cash, promissory notes, or assumption of indebtedness.

In March 2011, in connection with a loan and security agreement entered into with Comerica, we issued to Comerica a warrant to purchase 15,957 shares of our Series C redeemable convertible preferred stock. The warrant contains provisions for the adjustment of the exercise price and the number of shares issuable upon the exercise of the warrant in the event of certain stock dividends, stock splits, recapitalizations, reclassifications, exchanges, substitutions, consolidations, combinations and other similar events. In addition, the number of shares of common stock issuable upon conversion of the shares of Series C redeemable convertible preferred stock underlying the warrant are subject to adjustment for certain dilutive issuances pursuant to our certificate of incorporation as in effect prior to the completion of this offering. The provision for adjustment upon dilutive issuances is an element of the preferred stock into which the warrant is currently exercisable. Upon completion of this offering, the warrant will become exercisable for 2,006 shares of common stock and will no longer be subject to adjustment for dilutive issuances because our common stock is not subject to any provision for adjustment for dilutive issuances. The warrant expires on March 18, 2021, unless the Company is acquired prior to that time in a transaction in which the consideration paid by the acquirer is comprised solely of cash, promissory notes, or assumption of indebtedness. Both of our loan and security agreements with Comerica terminated upon our full repayment of all outstanding obligations under the agreements.

In July 2013, in connection with an amendment to a loan and security agreement entered into with Silicon Valley Bank, or SVB, we issued to SVB a warrant to purchase 59,312 shares of our Series D redeemable convertible preferred stock. Upon the funding of an additional tranche of financing, the number of shares exercisable under the warrant increased to 118,624. The warrant has a net exercise provision and contains provisions for the adjustment of the exercise price and the number of shares issuable upon the exercise of the warrant in the event of certain stock dividends, stock splits, reclassifications, exchanges, combinations, substitutions, replacements or other similar events. In addition, the number of shares of common stock issuable upon conversion of the shares of Series D redeemable convertible preferred stock underlying the warrant are subject to adjustment for certain dilutive issuances pursuant to our certificate of incorporation as in effect prior to the completion of this offering. The provision for adjustment upon dilutive issuances is an element of the preferred stock into which the warrant is currently exercisable. Upon the completion of this offering, the warrant will become exercisable for 14,913 shares of common stock and will no longer be subject to adjustment for dilutive issuances because our common stock is not subject to any provision for adjustment for dilutive issuances. The warrant expires on July 24, 2023. If the warrant has not been exercised prior to July 24, 2023, upon the expiration date the warrant will be deemed to automatically be exercised on a net exercise basis.

Registration and Voting Rights

Upon the completion of this offering, the holders of approximately 16,292,431 shares of our common stock issuable upon the conversion of our redeemable convertible preferred stock, which we refer to as our registrable securities, are entitled to rights with respect to the registration of these securities under the Securities Act. These rights are provided under the terms of a registration and voting rights agreement between us and certain holders our common stock, Series A redeemable convertible preferred stock, Series B redeemable convertible preferred stock, Series B-2 redeemable convertible preferred stock, Series C redeemable convertible preferred stock, Series D redeemable convertible preferred stock and Series E redeemable convertible preferred stock. The registration rights agreement includes demand registration rights, short-form registration rights and piggyback registration rights. All fees, costs and expenses of underwritten registrations under these agreements will be borne by us and all selling expenses, including underwriting discounts and selling commissions, will be borne by the holders of the shares being registered.

Demand Registration Rights

Beginning 180 days after the completion of this offering, the holders of our registrable securities are entitled to demand registration rights. Under the terms of the registration and voting rights agreement, we will be required, upon the written request of holders of a majority of these securities, to use our best efforts to file a registration statement and use reasonable, diligent efforts to effect the registration of all or a portion of these shares for public resale. We are required to effect only two registrations pursuant to this provision of the registration rights agreement.

Short-Form Registration Rights

Upon the completion of this offering, the holders of our registrable securities are also entitled to short form registration rights. Pursuant to the registration and voting rights agreement, if we are eligible to file a registration statement on Form S-3, upon the written request of holders of at least 10% of our registrable securities then outstanding to sell registrable securities at an aggregate price of at least $1.0 million, we will be required to use our best efforts to effect a registration of such shares. We are not required to keep effective at any one time more than three registration statements pursuant to this provision of the registration rights agreement.

Piggyback Registration Rights

Upon the completion of this offering, the holders of our registrable securities are entitled to piggyback registration rights. If we register any of our securities either for our own account or for the account of other

security holders, the holders of these shares are entitled to include their shares in the registration. Subject to certain exceptions contained in the registration and voting rights agreement, we and the underwriters may limit the number of shares included in the underwritten offering if the underwriters determine in good faith that marketing factors require a limitation of the number of shares to be underwritten.

Indemnification

Our registration and voting rights agreement contains customary cross-indemnification provisions, under which we are obligated to indemnify holders of registrable securities in the event of material misstatements or omissions in the registration statement attributable to us, and they are obligated to indemnify us for material misstatements or omissions attributable to them.

Expiration of Registration Rights

The demand registration rights and short form registration rights granted under the registration and voting rights agreement will terminate on the seventh anniversary of the completion of this offering.

Right of First Offer

Our registration and voting rights agreement provides certain holders of our capital stock who previously held our Series E redeemable convertible preferred stock prior to the completion of this offering with a right of first offer after March 31, 2016 with respect to any proposed sales of our common stock or securities convertible into or exercisable or exchangeable for, our common stock pursuant to a public offering registered under the Securities Act. This right of first offer entitles such holders to purchase, upon the same terms and conditions as other purchasers in the proposed sale, a percentage of our securities in proportion to the amount of our securities currently held by such holders, subject to certain limitations contained in the registration and voting rights agreement. Such rights will terminate upon the earliest of (i) two years from the closing of this offering, (ii) March 31, 2018, (iii) the time when such holders no longer hold at least 50% of the shares of Series E redeemable convertible preferred stock (or at least 50% of the shares of common stock issued upon conversion of such preferred stock) initially purchased by such holders, and (iv) upon the consummation of a liquidation, merger, consolidation, change in control, or sale of all or substantially all of our assets.

Board Designation Rights

Beginning upon the completion of this offering, certain holders of our capital stock who previously held our Series E redeemable convertible preferred stock prior to the completion of this offering may designate one individual as a nominee to serve on our board of directors, which rights will terminate upon the earliest of (i) two years from the closing of this offering, (ii) the time when such holders no longer hold at least 50% of the shares of Series E redeemable convertible preferred stock (or at least 50% of the shares of common stock issued upon conversion of such preferred stock) initially purchased by such holders, and (iii) upon the consummation of a liquidation, merger, consolidation, change in control, or sale of all or substantially all of our assets.

Anti-Takeover Effects of our Certificate of Incorporation and Bylaws and Delaware Law

Our certificate of incorporation and bylaws include a number of provisions that may have the effect of delaying, deferring or preventing another party from acquiring control of us and encouraging persons considering unsolicited tender offers or other unilateral takeover proposals to negotiate with our board of directors rather than pursue non-negotiated takeover attempts. These provisions include the items described below.

Board Composition and Filling Vacancies

Our 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 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. The classification of directors, together with the limitations on removal of directors and treatment of vacancies, has the effect of making it more difficult for stockholders to change the composition of our board of directors.

No Written Consent of Stockholders

Our 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. This limit may lengthen the amount of time required to take stockholder actions and would prevent the amendment of our bylaws or removal of directors by our stockholders without holding a meeting of stockholders.

Meetings of Stockholders

Our certificate of incorporation and 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 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 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 bylaws specify the requirements as to form and content of all stockholders' notices. These requirements may preclude stockholders from bringing matters before the stockholders at an annual or special meeting.

Amendment to Certificate of Incorporation and Bylaws

Any amendment of our certificate of incorporation must first be approved by a majority of our board of directors, and if required by law or our 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 bylaws and 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 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 certificate of incorporation provides for 7,285,456 authorized shares of preferred stock, of which 5,000,000 shares have been authorized as undesignated preferred stock. Our designated Series B redeemable

convertible preferred stock, Series C redeemable convertible preferred stock, and Series D redeemable convertible 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.

Section 203 of the Delaware General Corporation Law

Upon completion of this offering, we will be subject to the provisions of Section 203 of the Delaware General Corporation Law. 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, our 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, but not the outstanding voting stock owned by the interested stockholder; or
- at or after the time the stockholder became interested, the business combination was approved by our board of directors 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 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.

Exchange Listing

Our common stock has been approved for listing on The NASDAQ Global Select Market under the trading symbol “LIFE.”

Transfer Agent and Registrar

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

SHARES ELIGIBLE FOR FUTURE SALE

Prior to this offering, there has been no public market for our shares. Future sales of our common stock in the public market, or the availability of such shares for sale in the public market, could adversely affect market prices prevailing from time to time. As described below, only a limited number of shares will be available for sale shortly after this offering due to contractual and legal restrictions on resale. Nevertheless, sales of our common stock in the public market after such restrictions lapse, or the perception that those sales may occur, could adversely affect the prevailing market price at such time and our ability to raise equity capital in the future.

Based on the number of shares outstanding as of December 31, 2014, upon the completion of this offering, 22,549,739 shares of our common stock will be outstanding, assuming no exercise of the underwriters' option to purchase additional shares and no exercise of outstanding options or warrants. Of the outstanding shares, all of the shares sold in this offering will be freely tradable, except that any shares held by our affiliates, as that term is defined in Rule 144 under the Securities Act, may only be sold in compliance with the limitations described below.

As a result of the lock-up agreements described below and the provisions of Rule 144 and Rule 701 under the Securities Act, the shares of our common stock (excluding the shares sold in this offering) that will be available for sale in the public market are as follows:

Date of Availability of Sale	Approximate Number of Shares
As of the date of this prospectus	221,793
90 days after the date of this prospectus	221,812
180 days after the date of this prospectus, although a portion of such shares held by our affiliates will be subject to volume limitations pursuant to Rule 144	17,189,739

Rule 144

In general, a person who has beneficially owned restricted stock for at least six months would be entitled to sell their securities provided that (i) such person is not deemed to have been one of our affiliates at the time of, or at any time during the 90 days preceding, a sale and (ii) we are subject to the Exchange Act periodic reporting requirements for at least 90 days before the sale. Persons who have beneficially owned restricted shares for at least six months but who are our affiliates at the time of, or any time during the 90 days preceding, a sale, would be subject to additional restrictions, by which such person would be entitled to sell within any three-month period only a number of securities that does not exceed the greater of either of the following:

- 1% of the number of shares then outstanding, which will equal approximately 225,497 shares immediately after this offering assuming no exercise of the underwriters' option to purchase additional shares, based on the number of shares outstanding as of December 31, 2014; or
- the average weekly trading volume of our common stock on The NASDAQ Global Select Market during the four calendar weeks preceding the filing of a notice on Form 144 with respect to the sale;

provided, in each case, that we are subject to the Exchange Act periodic reporting requirements for at least 90 days before the sale. Such sales both by affiliates and by non-affiliates must also comply with the manner of sale, current public information and notice provisions of Rule 144.

Rule 701

Rule 701 under the Securities Act, as in effect on the date of this prospectus, permits resales of shares in reliance upon Rule 144 but without compliance with certain restrictions of Rule 144, including the holding period requirement. Most of our employees, executive officers or directors who purchased shares under a written compensatory plan or contract may be entitled to rely on the resale provisions of Rule 701, but all holders of

Rule 701 shares are required to wait until 90 days after the date of this prospectus before selling their shares. However, substantially all Rule 701 shares are subject to lock-up agreements as described below and under "Underwriting" included elsewhere in this prospectus and will become eligible for sale upon the expiration of the restrictions set forth in those agreements.

Lock-Up Agreements

All of our directors and executive officers and substantially all holders of our shares, who collectively hold 16,995,289 shares of common stock (including shares of common stock issuable upon the conversion of shares of our redeemable convertible preferred stock), have signed a lock-up agreement which prevents them from selling any of our common stock or any securities convertible into or exercisable or exchangeable for common stock for a period of not less than 180 days from the date of this prospectus without the prior written consent of the representatives, subject to certain exceptions. See "Underwriting."

Rule 10b5-1 Trading Plans

Following the closing of this offering, certain of our officers and directors may adopt written plans, known as Rule 10b5-1 trading plans, in which they will contract with a broker to buy or sell shares of our common stock on a periodic basis to diversify their assets and investments. Under these 10b5-1 trading plans, a broker may execute trades pursuant to parameters established by the officer or director when entering into the plan, without further direction from such officer or director. Such sales would not commence until the expiration of the applicable lock-up agreements entered into by such officer or director in connection with this offering.

Registration Rights

Upon completion of this offering, certain holders of our securities will be entitled to various rights with respect to registration of their shares under the Securities Act. Registration of these shares under the Securities Act would result in these shares becoming fully tradable without restriction under the Securities Act immediately upon the effectiveness of the registration. See "Description of Capital Stock—Registration Rights" for additional information.

Equity Incentive Plans

We intend to file one or more registration statements on Form S-8 under the Securities Act to register our shares issued or reserved for issuance under our equity incentive plans. The first such registration statement is expected to be filed soon after the date of this prospectus and will automatically become effective upon filing with the Securities and Exchange Commission. Accordingly, shares registered under such registration statement will be available for sale in the open market, unless such shares are subject to vesting restrictions with us or the lock-up restrictions described above. As of May 6, 2015, we estimate that such registration statement on Form S-8 will cover approximately 3,793,778 shares.

CERTAIN MATERIAL UNITED STATES FEDERAL INCOME TAX CONSIDERATIONS FOR NON-U.S. HOLDERS

The following is a summary of certain material U.S. federal income tax considerations of the ownership and disposition of our common stock to non-U.S. holders (as defined below). It is not intended to be a complete analysis of all the U.S. federal income tax considerations that may be relevant to non-U.S. holders. This summary is based upon the provisions of the Internal Revenue Code, or the Code, Treasury regulations promulgated thereunder, administrative rulings and judicial decisions, all as of the date hereof. These authorities may be changed, possibly with retroactive effect, which may result in U.S. federal income tax consequences different from those set forth below. We have not sought any ruling from the Internal Revenue Service, or IRS, with respect to the statements made and the conclusions reached in the following summary. There can be no assurance that the IRS will agree with such statements and conclusions or that any contrary position taken by the IRS would not be sustained by a court.

This summary also does not address alternative minimum tax consequences, estate or gift tax consequences, or the tax considerations arising under the laws of any foreign, state or local jurisdiction. In addition, this discussion does not address tax considerations applicable to an investor's particular circumstances or to investors that may be subject to special tax rules, including, without limitation:

- banks, insurance companies or other financial institutions;
- tax-exempt organizations;
- an integral part or controlled entity of a foreign sovereign;
- dealers in securities or currencies;
- traders in securities that elect to use a mark-to-market method of accounting for their securities holdings;
- persons that own, or are deemed to own, more than five percent of our capital stock (except to the extent specifically set forth below);
- controlled foreign corporations or passive foreign investment companies
- certain former citizens or long-term residents of the United States;
- persons who hold our common stock as a position in a hedging transaction, "straddle," "conversion transaction" or other risk reduction transaction;
- persons deemed to sell our common stock under the constructive sale provisions of the Code;
- an entity that is treated as a partnership for U.S. federal income tax purposes; or
- persons who hold our common stock other than as a capital asset (generally, an asset held for investment purposes).

If a partnership holds our common stock, the tax treatment of a partner generally will depend on the status of the partner and upon the activities of the partnership. Accordingly, partnerships that hold our common stock, and partners in such partnerships, should consult their tax advisors.

YOU ARE URGED TO CONSULT YOUR TAX ADVISOR WITH RESPECT TO THE APPLICATION OF THE UNITED STATES FEDERAL INCOME TAX LAWS TO YOUR PARTICULAR SITUATION, AS WELL AS ANY TAX CONSEQUENCES OF THE PURCHASE, OWNERSHIP AND DISPOSITION OF OUR COMMON STOCK ARISING UNDER THE UNITED STATES FEDERAL ESTATE OR GIFT TAX RULES OR UNDER THE LAWS OF ANY STATE, LOCAL, FOREIGN OR OTHER TAXING JURISDICTION OR UNDER ANY APPLICABLE TAX TREATY.

Non-U.S. Holder Defined

For purposes of this discussion, a "non-U.S. holder" is a beneficial owner of a share of common stock received that is (i) a foreign corporation, (ii) a nonresident alien individual, or (iii) a foreign trust or a foreign estate that is not subject to United States federal income tax on a net income basis.

Distributions

We have not made any distributions on our common stock and do not plan to make any distributions for the foreseeable future. However, if we do make distributions on our common stock, those payments will constitute dividends for U.S. tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. To the extent those distributions exceed both our current and our accumulated earnings and profits, they will constitute a return of capital and will first reduce your basis in our common stock, but not below zero, and then will be treated as gain from the sale of stock, which will be subject to tax as described in "Gain on Disposition of Common Stock", below.

Any dividend paid to you generally will be subject to U.S. withholding tax either at a rate of 30% of the gross amount of the dividend or such lower rate as may be specified by an applicable income tax treaty. In order to receive a reduced treaty rate, you must provide us with an IRS Form W-8BEN, IRS Form W-8BEN-E, or other appropriate version of IRS Form W-8 or successor form certifying qualification for the reduced rate.

Dividends received by you that are effectively connected with your conduct of a U.S. trade or business and, if required by an applicable income tax treaty, are attributable to a U.S. permanent establishment, are exempt from such withholding tax. In order to obtain this exemption, you must provide us with an IRS Form W-8ECI or successor form properly certifying such exemption. Such effectively connected dividends, although not subject to withholding tax, are taxed at the same graduated rates applicable to U.S. persons, net of certain deductions and credits. In addition, if you are a corporate non-U.S. holder, dividends you receive that are effectively connected with your conduct of a U.S. trade or business may also be subject to a branch profits tax at a rate of 30% or such lower rate as may be specified by an applicable income tax treaty. Non-U.S. holders are urged to consult their tax advisers regarding their entitlement to benefits under an applicable income tax treaty.

If you are eligible for a reduced rate of withholding tax pursuant to a tax treaty, you may obtain a refund of any excess amounts withheld if you file an appropriate claim for refund with the IRS.

Gain on Disposition of Common Stock

Subject to the discussions below regarding backup withholding and FATCA (as defined below), you generally will not be subject to U.S. federal income tax on any gain realized upon the sale or other disposition of our common stock unless:

- the gain is effectively connected with your conduct of a U.S. trade or business and, if required by an applicable income tax treaty, is attributable to a U.S. permanent establishment;
- you are an individual non-U.S. holder who holds our common stock as a capital asset, you are present in the United States for a period or periods aggregating 183 days or more during the calendar year in which the sale or disposition occurs and certain other conditions are met; or
- our common stock constitutes a U.S. real property interest by reason of our status as a "United States real property holding corporation" for U.S. federal income tax purposes, or USRPHC, at any time within the shorter of the five-year period preceding the disposition or your holding period for our common stock.

If you are a non-U.S. holder described in the first bullet above, you will be required to pay tax on the net gain derived from the sale under regular graduated U.S. federal income tax rates. Corporate non-U.S. holders described in the first bullet above may be subject to the branch profits tax at a 30% rate or such lower rate as may be specified by an applicable income tax treaty. If you are an individual non-U.S. holder described in the second

bullet above, you will be required to pay a flat 30% tax on the gain derived from the sale, which may be offset by U.S.-source capital losses (even though you are not considered a resident of the United States) provided that you have timely filed a federal income tax return with respect to such losses. You should consult any applicable income tax or other treaties, which may provide different rules.

We believe that we are not currently and will not become a USRPHC. However, because the determination of whether we are a USRPHC depends on the fair market value of our U.S. real property relative to the fair market value of our other business assets, there can be no assurance that we will not become a USRPHC in the future. Even if we become a USRPHC, however, as long as our common stock is regularly traded on an established securities market, such common stock will be treated as U.S. real property interests only if you actually or constructively hold more than five percent of such regularly traded common stock at any time during the shorter of the five-year period preceding the disposition or your holding period for our common stock.

Backup Withholding and Information Reporting

Generally, we must report annually to the IRS the amount of dividends paid to you, your name and address, and the amount of tax withheld, if any. A similar report will be sent to you. Pursuant to applicable income tax treaties or other agreements, the IRS may make these reports available to tax authorities in your country of residence.

Payments of dividends or of proceeds on the disposition of stock made to you may be subject to additional information reporting and backup withholding (currently at a rate of 28%) unless you establish an exemption, for example by properly certifying your non-U.S. status on a Form W-8BEN, Form W-8BEN-E, or another appropriate version of IRS Form W-8 or successor form. Notwithstanding the foregoing, backup withholding and information reporting may apply if the applicable withholding agent has actual knowledge, or reason to know, that you are a U.S. person.

Backup withholding is not an additional tax; rather, the U.S. income tax liability of persons subject to backup withholding will be reduced by the amount of tax withheld. If withholding results in an overpayment of taxes, a refund or credit may be obtained, provided that the required information is furnished to the IRS in a timely manner.

FATCA

Legislation known as the Foreign Account Tax Compliance Act and guidance issued thereunder (together, FATCA) imposes withholding taxes on certain types of payments made to “foreign financial institutions” and certain other non-U.S. entities (including financial intermediaries). FATCA imposes a 30% withholding tax on certain payments of dividends, and, for dispositions that occur on or after January 1, 2017, the gross proceeds from such dispositions of our common stock paid to a foreign financial institution or to certain non-financial foreign entities unless certain certification, information reporting and other specified requirements are met or an exemption applies. Prospective investors should consult their tax advisors regarding FATCA.

UNDERWRITING

We are offering the shares of common stock described in this prospectus through a number of underwriters. J.P. Morgan Securities LLC and Citigroup Global Markets Inc. are acting as joint book-running managers of the offering and as representatives of the underwriters. We have entered into an underwriting agreement with the underwriters. Subject to the terms and conditions of the underwriting agreement, we have agreed to sell to the underwriters, and each underwriter has severally agreed to purchase, at the public offering price less the underwriting discounts and commissions set forth on the cover page of this prospectus, the number of shares of common stock listed next to its name in the following table:

Name	Number of Shares
J.P. Morgan Securities LLC	2,144,000
Citigroup Global Markets Inc.	1,661,600
BMO Capital Markets Corp.	1,072,000
William Blair & Company, L.L.C.	482,400
Total	5,360,000

The underwriters are committed to purchase all the common shares offered by us if they purchase any shares. The underwriting agreement also provides that if an underwriter defaults, the purchase commitments of non-defaulting underwriters may also be increased or the offering may be terminated.

The underwriters propose to offer the common shares directly to the public at the initial public offering price set forth on the cover page of this prospectus and to certain dealers at that price less a concession not in excess of $0.5880 per share. After the initial offering of the shares to the public, the offering price and other selling terms may be changed by the underwriters. Sales of shares made outside of the United States may be made by affiliates of the underwriters.

The underwriters have an option to buy up to 804,000 additional shares of common stock from us to cover sales by the underwriters which exceed the number of shares specified in the table above. The underwriters have 30 days from the date of this prospectus to exercise this option to purchase additional shares. If any shares are purchased with this option to purchase additional shares, the underwriters will purchase shares in approximately the same proportion as shown in the table above. If any additional shares of common stock are purchased, the underwriters will offer the additional shares on the same terms as those on which the shares are being offered.

The underwriting fee is equal to the public offering price per share of common stock less the amount paid by the underwriters to us per share of common stock. The underwriting fee is $0.98 per share. The following table shows the per share and total underwriting discounts and commissions to be paid to the underwriters assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

	Without option to purchase additional shares exercise	With full option to purchase additional shares exercise
Per share	$ 0.98	$ 0.98
Total	$ 5,252,800	$ 6,040,720

We estimate that the total expenses of this offering, including registration, filing and listing fees, printing fees and legal and accounting expenses, but excluding the underwriting discounts and commissions, will be approximately $3.4 million. We have agreed to reimburse the underwriters for expenses of $50,000 relating to the clearance of this offering with the Financial Industry Regulatory Authority.

A prospectus in electronic format may be made available on the web sites maintained by one or more underwriters or selling group members, if any, participating in the offering. The underwriters may agree to allocate a number of shares to underwriters and selling group members for sale to their online brokerage account holders. Internet distributions will be allocated by the representatives to underwriters and selling group members that may make Internet distributions on the same basis as other allocations.

We have agreed that we will not (i) offer, pledge, announce the intention to sell, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase or otherwise dispose of, directly or indirectly, or file with the Securities and Exchange Commission, or SEC, a registration statement under the Securities Act of 1933, or Securities Act, relating to, any shares of our common stock or securities convertible into or exchangeable or exercisable for any shares of our common stock, or publicly disclose the intention to make any offer, sale, pledge, disposition or filing, or (ii) enter into any swap or other arrangement that transfers all or a portion of the economic consequences associated with the ownership of any shares of common stock or any such other securities (regardless of whether any of these transactions are to be settled by the delivery of shares of common stock or such other securities, in cash or otherwise), in each case without the prior written consent of J.P. Morgan Securities LLC and Citigroup Global Markets Inc. for a period of 180 days after the date of this prospectus (the "restricted period"), other than the shares of our common stock to be sold hereunder and any shares of our common stock issued upon the exercise of options granted under our existing stock-based compensation plans.

Our directors, executive officers and substantially all of our equity holders have entered into lock-up agreements with the underwriters prior to the commencement of this offering pursuant to which each of these persons or entities, with limited exceptions, during the restricted period, may not, without the prior written consent of J.P. Morgan Securities LLC and Citigroup Global Markets Inc., (1) offer, pledge, announce the intention to sell, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, or otherwise transfer or dispose of, directly or indirectly, any shares of our common stock or any securities convertible into or exercisable or exchangeable for our common stock (including, without limitation, common stock or such other securities which may be deemed to be beneficially owned by such directors, executive officers, managers and members in accordance with the rules and regulations of the SEC and securities which may be issued upon exercise of a stock option or warrant) or (2) enter into any swap or other agreement that transfers, in whole or in part, any of the economic consequences of ownership of the common stock or such other securities, whether any such transaction described in clause (1) or (2) above is to be settled by delivery of common stock or such other securities, in cash or otherwise, or (3) make any demand for or exercise any right with respect to the registration of any shares of our common stock or any security convertible into or exercisable or exchangeable for our common stock.

The restrictions described above are subject to certain exceptions, including for (i) transfers by our stockholders of our common stock (or any security convertible into or exercisable or exchangeable for our common stock) pursuant to a bona fide third party tender offer, merger, consolidation or other similar transaction approved by our board of directors and made to all holders of our common stock involving a "change in control" and (ii) the issuance of securities by us in connection with a transaction with an unaffiliated third party that includes a bona fide commercial relationship (including joint ventures, marketing or distribution arrangements, collaboration agreements or intellectual property license agreements) or any acquisition of assets or acquisition of not less than a majority or controlling portion of the equity of another entity, provided that the aggregate number of shares issued shall not exceed 5% of the total number of outstanding shares of common stock immediately following the completion of this offering and provided that the recipient of the securities enters into a lock-up agreement with the underwriters for the remainder of the restricted period.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act.

Our common stock has been approved for listing on The NASDAQ Global Select Market under the symbol "LIFE."

In connection with this offering, the underwriters may engage in stabilizing transactions, which involves making bids for, purchasing and selling shares of common stock in the open market for the purpose of preventing or retarding a decline in the market price of the common stock while this offering is in progress. These stabilizing transactions may include making short sales of the common stock, which involves the sale by the underwriters of a greater number of shares of common stock than they are required to purchase in this offering, and purchasing shares of common stock on the open market to cover positions created by short sales. Short sales may be "covered" shorts, which are short positions in an amount not greater than the underwriters' option to purchase additional shares referred to above, or may be "naked" shorts, which are short positions in excess of that amount. The underwriters may close out any covered short position either by exercising their option to purchase additional shares, in whole or in part, or by purchasing shares in the open market. In making this determination, the underwriters will consider, among other things, the price of shares available for purchase in the open market compared to the price at which the underwriters may purchase shares through the option to purchase additional shares. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market that could adversely affect investors who purchase in this offering. To the extent that the underwriters create a naked short position, they will purchase shares in the open market to cover the position.

The underwriters have advised us that, pursuant to Regulation M of the Securities Act of 1933, they may also engage in other activities that stabilize, maintain or otherwise affect the price of the common stock, including the imposition of penalty bids. This means that if the representatives of the underwriters purchase common stock in the open market in stabilizing transactions or to cover short sales, the representatives can require the underwriters that sold those shares as part of this offering to repay the underwriting discount received by them.

These activities may have the effect of raising or maintaining the market price of the common stock or preventing or retarding a decline in the market price of the common stock, and, as a result, the price of the common stock may be higher than the price that otherwise might exist in the open market. If the underwriters commence these activities, they may discontinue them at any time. The underwriters may carry out these transactions on The NASDAQ Global Select Market, in the over-the-counter market or otherwise.

Prior to this offering, there has been no public market for our common stock. The initial public offering price was determined by negotiations between us and the representatives of the underwriters. In determining the initial public offering price, we and the representatives of the underwriters considered a number of factors including:

- the information set forth in this prospectus and otherwise available to the representatives;
- our prospects and the history and prospects for the industry in which we compete;
- an assessment of our management;
- our prospects for future earnings;
- the general condition of the securities markets at the time of this offering;
- the recent market prices of, and demand for, publicly traded common stock of generally comparable companies; and
- other factors deemed relevant by the underwriters and us.

Neither we nor the underwriters can assure investors that an active trading market will develop for our common shares, or that the shares will trade in the public market at or above the initial public offering price.

Selling Restrictions

General

Other than in the United States, no action has been taken by us or the underwriters that would permit a public offering of the securities offered by this prospectus in any jurisdiction where action for that purpose is required. The securities offered by this prospectus may not be offered or sold, directly or indirectly, nor may this prospectus or any other offering material or advertisements in connection with the offer and sale of any such securities be distributed or published in any jurisdiction, except under circumstances that will result in compliance with the applicable rules and regulations of that jurisdiction. Persons into whose possession this prospectus comes are advised to inform themselves about and to observe any restrictions relating to the offering and the distribution of this prospectus. This prospectus does not constitute an offer to sell or a solicitation of an offer to buy any securities offered by this prospectus in any jurisdiction in which such an offer or a solicitation is unlawful.

European Economic Area

In relation to each Member State of the European Economic Area (each, a "Relevant Member State"), no offer of shares may be made to the public in that Relevant Member State other than:

- to any legal entity which is a qualified investor as defined in the Prospectus Directive;
- to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the representatives; or
- in any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer of shares shall require the Company or the representatives to publish a prospectus pursuant to Article 3 of the Prospectus Directive or supplement a prospectus pursuant to Article 16 of the Prospectus Directive.

Each person in a Relevant Member State who initially acquires any shares or to whom any offer is made will be deemed to have represented, acknowledged and agreed that it is a "qualified investor" within the meaning of the law in that Relevant Member State implementing Article 2(1)(e) of the Prospectus Directive. In the case of any shares being offered to a financial intermediary as that term is used in Article 3(2) of the Prospectus Directive, each such financial intermediary will be deemed to have represented, acknowledged and agreed that the shares acquired by it in the offer have not been acquired on a non-discretionary basis on behalf of, nor have they been acquired with a view to their offer or resale to, persons in circumstances which may give rise to an offer of any shares to the public other than their offer or resale in a Relevant Member State to qualified investors as so defined or in circumstances in which the prior consent of the representatives has been obtained to each such proposed offer or resale.

The Company, the representatives and their affiliates will rely upon the truth and accuracy of the foregoing representations, acknowledgements and agreements.

This prospectus has been prepared on the basis that any offer of shares in any Relevant Member State will be made pursuant to an exemption under the Prospectus Directive from the requirement to publish a prospectus for offers of shares. Accordingly any person making or intending to make an offer in that Relevant Member State of shares which are the subject of the offering contemplated in this prospectus may only do so in circumstances in which no obligation arises for the Company or any of the underwriters to publish a prospectus pursuant to Article 3 of the Prospectus Directive in relation to such offer. Neither the Company nor the underwriters have authorized, nor do they authorize, the making of any offer of shares in circumstances in which an obligation arises for the Company or the underwriters to publish a prospectus for such offer.

For the purpose of the above provisions, 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 the shares to be offered so as to enable an investor to decide to purchase or subscribe the shares, as the same may be varied in the Relevant Member State by any measure implementing the Prospectus Directive in the Relevant Member State and the expression "Prospectus Directive" means Directive 2003/71/EC (including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member States) and includes any relevant implementing measure in the Relevant Member State and the expression "2010 PD Amending Directive" means Directive 2010/73/EU.

United Kingdom

In the United Kingdom, this document is being distributed only to, and is directed only at, and any offer subsequently made may only be directed at persons who are "qualified investors" (as defined in the Prospectus Directive) (i) who have professional experience in matters relating to investments falling within Article 19 (5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended (the "Order") and/or (ii) who are high net worth companies (or persons to whom it may otherwise be lawfully communicated) falling within Article 49(2)(a) to (d) of the Order (all such persons together being referred to as "relevant persons").

Any person in the United Kingdom that is not a relevant person should not act or rely on the information included in this document or use it as basis for taking any action. In the United Kingdom, any investment or investment activity that this document relates to may be made or taken exclusively by relevant persons. Any person in the United Kingdom that is not a relevant person should not act or rely on this document or any of its contents.

Switzerland

The shares may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange, or the SIX, or on any other stock exchange or regulated trading facility in Switzerland. This document does not constitute a prospectus within the meaning of, and has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this document nor any other offering or marketing material relating to the shares or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this document nor any other offering or marketing material relating to the offering, the Company, or the shares have been or will be filed with or approved by any Swiss regulatory authority. In particular, this document will not be filed with, and the offer of shares will not be supervised by, the Swiss Financial Market Supervisory Authority FINMA, and the offer of shares has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes, or the CISA. The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of shares.

Hong Kong

The shares have not been offered or sold and will not be offered or sold in Hong Kong, by means of any document, other than (a) to "professional investors" as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance; or (b) in other circumstances which do not result in the document being a "prospectus" as defined in the Companies Ordinance (Cap. 32) of Hong Kong or which do not constitute an offer to the public within the meaning of that Ordinance. No advertisement, invitation or document relating to the shares has been or may be issued or has been or may be in the possession of any person for the purposes of issue, whether in Hong Kong or elsewhere, which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted to do so under the securities laws

of Hong Kong) other than with respect to shares which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" as defined in the Securities and Futures Ordinance and any rules made thereunder.

Singapore

This prospectus has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale or invitation for subscription or purchase, of shares may not be circulated or distributed, nor may the shares be offered or sold or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore, or SFA, (ii) to a relevant person pursuant to Section 275(1), or any person pursuant to Section 275(1A), and in accordance with the conditions specified in Section 275, of the SFA, or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the shares are subscribed or purchased under Section 275 of the SFA by a relevant person which is: (a) a corporation (which is not an accredited investor (as defined in Section 4A of the SFA)) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or (b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of the trust is an individual who is an accredited investor, securities (as defined in Section 239(1) of the SFA) of that corporation or the beneficiaries' rights and interest (howsoever described) in that trust shall not be transferred within six months after that corporation or that trust has acquired the shares pursuant to an offer made under Section 275 of the SFA except: (1) to an institutional investor or to a relevant person defined in Section 275(2) of the SFA, or to any person arising from an offer referred to in Section 275(1A) or Section 276(4)(i)(B) of the SFA; (2) where no consideration is or will be given for the transfer; (3) where the transfer is by operation of law; (4) as specified in Section 276(7) of the SFA; or (5) as specified in Regulation 32 of the Securities and Futures (Offers of Investments) (Shares and Debentures) Regulations 2005 of Singapore.

Japan

The shares have not been and will not be registered under the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948, as amended) and, accordingly, will not be offered or sold, directly or indirectly, in Japan, or for the benefit of any Japanese Person or to others for re-offering or resale, directly or indirectly, in Japan or to any Japanese Person, except in compliance with all applicable laws, regulations and ministerial guidelines promulgated by relevant Japanese governmental or regulatory authorities in effect at the relevant time. For the purposes of this paragraph, "Japanese Person" shall mean any person resident in Japan, including any corporation or other entity organized under the laws of Japan.

Qatar

The shares described in this prospectus have not been, and will not be, offered, sold or delivered, at any time, directly or indirectly in the State of Qatar in a manner that would constitute a public offering. This prospectus has not been, and will not be, registered with or approved by the Qatar Financial Markets Authority or Qatar Central Bank and may not be publicly distributed. This prospectus is intended for the original recipient only and must not be provided to any other person. It is not for general circulation in the State of Qatar and may not be reproduced or used for any other purpose.

Saudi Arabia

No offering, whether directly or indirectly, will be made to an investor in the Kingdom of Saudi Arabia unless such offering is in accordance with the applicable laws of the Kingdom of Saudi Arabia and the rules and regulations of the Capital Market Authority, including the Capital Market Law of the Kingdom of Saudi Arabia. The shares will not be marketed or sold in the Kingdom of Saudi Arabia by us or the underwriters.

This prospectus may not be distributed in the Kingdom of Saudi Arabia except to such persons as are permitted under the Office of Securities Regulation issued by the Capital Market Authority. The Saudi Arabian Capital Market Authority does not make any representation as to the accuracy or completeness of this prospectus and expressly disclaims any liability whatsoever for any loss arising from, or incurred in reliance upon, any part of this prospectus. Prospective purchasers of the shares offered hereby should conduct their own due diligence on the accuracy of the information relating to the shares. If you do not understand the contents of this prospectus, you should consult an authorized financial advisor.

United Arab Emirates

This offering has not been approved or licensed by the Central Bank of the United Arab Emirates (UAE), Securities and Commodities Authority of the UAE or any other relevant licensing authority in the UAE including any licensing authority incorporated under the laws and regulations of any of the free zones established and operating in the territory of the UAE, in particular the Dubai Financial Services Authority (DFSA), a regulatory authority of the Dubai International Financial Centre (DIFC). The offering does not constitute a public offer of securities in the UAE, DIFC or any other free zone in accordance with the Commercial Companies Law, Federal Law No. 8 of 1984 (as amended), DFSA Offered Securities Rules and NASDAQ Dubai Listing Rules, accordingly, or otherwise. The shares may not be offered to the public in the UAE or any of the free zones.

The shares may be offered and issued only to a limited number of investors in the UAE or any of its free zones who qualify as sophisticated investors under the relevant laws and regulations of the UAE or the free zone concerned.

Certain of the underwriters and their affiliates have provided in the past to us and our affiliates and may provide from time to time in the future certain commercial banking, financial advisory, investment banking and other services for us and such affiliates in the ordinary course of their business, for which they have received and may continue to receive customary fees and commissions. In addition, from time to time, certain of the underwriters and their affiliates may effect transactions for their own account or the account of customers, and hold on behalf of themselves or their customers, long or short positions in our debt or equity securities or loans, and may do so in the future.

LEGAL MATTERS

The validity of the shares of common stock offered by this prospectus will be passed upon for us by Goodwin Procter LLP, San Francisco, California. Certain legal matters will be passed upon for the underwriters by Davis Polk & Wardwell LLP, Menlo Park, California.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, has audited our consolidated financial statements at December 31, 2013 and 2014 and for each of the two years in the period ended December 31, 2014, as set forth in their report. We have included our financial statements in the prospectus and elsewhere in the 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 Securities and Exchange Commission, or SEC, a registration statement on Form S-1 (File Number 333-203272) under the Securities Act of 1933, or the Securities Act, with respect to the common stock we are offering by this prospectus. This prospectus does not contain all of the information included in the registration statement. For further information pertaining to us and our common stock, you should refer to the registration statement and to its exhibits. Whenever we make reference in this prospectus to any of our contracts, agreements or other documents, the references are not necessarily complete, and you should refer to the exhibits attached to the registration statement for copies of the actual contract, agreement or other document.

Upon the completion of the offering, we will be subject to the informational requirements of the Securities Exchange Act of 1934, or the Exchange Act, and will file annual, quarterly and current reports, proxy statements and other information with the SEC. You can read our SEC filings, including the registration statement, over the Internet at the SEC's website at www.sec.gov. You may also read and copy any document we file with the SEC at its public reference facility at 100 F Street, N.E., Room 1580, Washington, D.C. 20549. We also maintain a website at www.atyrpharma.com. Upon completion of the offering, you may access, free of charge, our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendment to those reported filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act as soon as reasonably practicable after such material is electronically filed with, or furnished to, the SEC.

You may also obtain copies of the documents at prescribed rates by writing to the Public Reference Section of the SEC at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the operation of the public reference facilities.

aTyr Pharma, Inc.

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Report of Independent Registered Public Accounting Firm

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

We have audited the accompanying consolidated balance sheets of aTyr Pharma, Inc. as of December 31, 2013 and 2014, and the related consolidated statements of operations, redeemable convertible preferred stock and stockholders' equity (deficit) and cash flows for the years then ended. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. We were not engaged to perform an audit of the Company's internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of aTyr Pharma, Inc. at December 31, 2013 and 2014, and the consolidated results of its operations and its cash flows for the years then ended, in conformity with U.S. generally accepted accounting principles.

/s/ Ernst & Young LLP
San Diego, California
April 3, 2015,
except for paragraphs 7, 8 and 9 of Note 10, as to which the date is April 25, 2015
and except for paragraph 10 of Note 10, as to which the date is May 5, 2015

aTyr Pharma, Inc.

Consolidated Balance Sheets
(in thousands, except share and per share data)

	December 31,		Pro Forma December 31,
	2013	2014	2014
Assets			(unaudited)
Current assets:			
Cash and cash equivalents	$ 36,457	$ 13,899	
Investment securities	-	1,954	
Prepaid expenses and other assets	564	656	
Total current assets	37,021	16,509	
Property and equipment, net	2,505	1,925	
Other assets	260	2,210	
Total assets	$ 39,786	$ 20,644	
Liabilities, Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit)			
Current liabilities:			
Accounts payable	$ 1,055	$ 1,433	
Accrued expenses	2,941	2,932	
Current portion of deferred rent	276	295	
Current portion of commercial bank debt	728	3,134	
Current portion of convertible promissory note	-	2,000	
Preferred stock warrant liabilities	207	319	$ -
Total current liabilities	5,207	10,113	
Deferred rent, net of current portion	741	445	
Commercial bank debt, net of current portion	4,158	5,142	
Convertible promissory note	2,000	-	
Other long-term liabilities	597	335	
Commitments and contingencies (Note 6)			
Redeemable convertible preferred stock, $0.001 par value; authorized shares - 75,772,871 at December 31, 2013 and 2014; issued and outstanding shares - 73,487,415 at December 31, 2013 and 2014; liquidation preference of $95,619 at December 31, 2013 and 2014; no shares issued and outstanding, pro forma (unaudited)	93,165	95,619	-
Stockholders' equity (deficit):			
Common stock, $0.001 par value; authorized shares - 94,000,000 at December 31, 2013 and 95,500,000 at December 31, 2014; issued and outstanding - 856,591 shares and 909,880 shares at December 31, 2013 and 2014, respectively; 10,148,748 shares issued and outstanding, pro forma (unaudited)	1	1	10
Additional paid-in capital	17,373	19,209	115,138
Stockholder note receivable	(69)	(69)	(69)
Accumulated deficit	(85,801)	(110,151)	(110,151)
Total stockholders' equity (deficit) of aTyr Pharma, Inc.	(68,496)	(91,010)	4,928
Noncontrolling interest	2,414	-	-
Total stockholders' equity (deficit)	(66,082)	(91,010)	$ 4,928
Total liabilities, redeemable convertible preferred stock and stockholders' equity (deficit)	$ 39,786	$ 20,644	

See accompanying notes.

aTyr Pharma, Inc.

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

	Years Ended December 31,	
	2013	**2014**
Operating expenses:		
Research and development	$ 13,832	$ 16,777
General and administrative	5,710	6,777
Total operating expenses	19,542	23,554
Loss from operations	(19,542)	(23,554)
Other income (expense):		
Interest expense, net	(444)	(832)
Change in fair value of warrant liabilities	(28)	36
Total other income (expense)	(472)	(796)
Net loss	(20,014)	(24,350)
Accretion to redemption value of redeemable convertible preferred stock	(1,637)	(416)
Net loss attributable to common stockholders	$ (21,651)	$ (24,766)
Net loss per share attributable to common stockholders, basic and diluted	$ (28.39)	$ (29.69)
Weighted average shares outstanding, basic and diluted	762,761	834,221
Pro forma net loss per share attributable to common stockholders, basic and diluted (unaudited)		$ (2.42)
Pro forma weighted average shares outstanding, basic and diluted (unaudited)		10,073,089

See accompanying notes.

aTyr Pharma, Inc.

Consolidated Statements of Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit)
(in thousands, except share data)

	Redeemable Convertible Preferred Stock		Common Stock		Additional Paid-in Capital	Stockholder Note Receivable	Accumulated Deficit	Non-Controlling Interest	Total Stockholders' Equity (Deficit)
	Shares	Amount	Shares	Amount					
Balance at December 31, 2012	55,211,585	$ 63,225	788,946	$ 1	$ 5	$ (69)	$ (64,516)	$ 25	$ (64,554)
Issuance of Series D redeemable convertible preferred stock for cash	14,504,841	36,683	-	-	-	-	-	2,431	2,431
Issuance of Series D redeemable convertible preferred stock for conversion of debt and accrued interest	3,770,989	9,537	-	-	-	-	-	-	-
Series D redeemable convertible preferred stock issuance costs	-	(389)	-	-	-	-	-	(65)	(65)
Exercise of common stock options	-	-	67,645	-	54	-	-	23	77
Vested shares related to repurchase liability, net	-	-	-	-	(3)	-	-	-	(3)
Stock-based compensation	-	-	-	-	155	-	-	-	155
Accretion to redemption value of redeemable convertible preferred stock	-	1,637	-	-	(366)	-	(1,271)	-	(1,637)
Capital contribution related to reversal of historical accretion of redeemable convertible preferred stock	-	(17,528)	-	-	17,528	-	-	-	17,528
Net loss	-	-	-	-	-	-	(20,014)	-	(20,014)
Balance at December 31, 2013	73,487,415	93,165	856,591	1	17,373	(69)	(85,801)	2,414	(66,082)
Exercise of common stock options	-	-	53,289	-	43	-	-	29	72
Vested shares related to repurchase liability	-	-	-	-	13	-	-	-	13
Stock-based compensation	-	-	-	-	1,791	-	-	-	1,791
Dissolution of Affiliates	-	2,038	-	-	405	-	-	(2,443)	(2,038)
Accretion to redemption value of redeemable convertible preferred stock	-	416	-	-	(416)	-	-	-	(416)
Net loss	-	-	-	-	-	-	(24,350)	-	(24,350)
Balance at December 31, 2014	73,487,415	$ 95,619	909,880	$ 1	$ 19,209	$ (69)	$ (110,151)	$ -	$ (91,010)

See accompanying notes.

aTyr Pharma, Inc.

Consolidated Statements of Cash Flows
(in thousands)

	Years Ended December 31,	
	2013	**2014**
Cash flows from operating activities		
Net loss	$(20,014)	$(24,350)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization	714	829
Stock-based compensation	155	1,791
Amortization of debt discount	211	426
Change in fair value of preferred stock warrant liability	28	(36)
Amortization of investment premium (discount)	-	43
Deferred rent	(254)	(277)
Changes in assets and liabilities:		
Prepaid expenses and other assets	323	(1,043)
Accounts payable and accrued expenses	1,526	(207)
Net cash used in operating activities	(17,311)	(22,824)
Cash flows from investing activities		
Purchase of property and equipment	(644)	(249)
Purchases of investment securities	-	(5,397)
Maturities of investment securities	-	3,400
Net cash used in investing activities	(644)	(2,246)
Cash flows from financing activities		
Issuance of preferred stock for cash, net of issuance costs	38,660	-
Proceeds from stock option exercises	77	72
Proceeds from commercial bank debt	5,000	5,000
Repayment of commercial bank debt	(2,500)	(1,561)
Proceeds from convertible debt	10,000	-
Repayment of convertible debt	(500)	-
Costs paid in connection with initial public offering	-	(999)
Net cash provided by financing activities	50,737	2,512
Net increase (decrease) in cash and cash equivalents	32,782	(22,558)
Cash at beginning of period	3,675	36,457
Cash at end of period	$ 36,457	$ 13,899
Supplemental disclosure of cash flow information		
Interest paid	$ 254	$ 415
Supplemental schedule of noncash investing and financing activities		
Issuance of warrants in connection with long-term debt	$ 137	$ 148
Change in unvested share liability	$ (3)	$ 13
Capital contribution related to reversal of historical accretion of redeemable convertible preferred stock	$ 17,528	$ -
Conversion of convertible debt and accrued interest	$ 9,537	$ -

See accompanying notes.

aTyr Pharma, Inc.

Notes to Consolidated Financial Statements

1. Organization, Business and Basis of Presentation

Organization and Business

aTyr Pharma, Inc. (the Company) was incorporated in the state of Delaware on September 8, 2005. The Company is focused on the discovery and clinical development of innovative medicines for patients suffering from severe rare diseases.

Principles of Consolidation

The consolidated financial statements include the accounts of aTyr Pharma, Inc., its 98% majority-owned subsidiary in Hong Kong, Pangu BioPharma Limited (Pangu BioPharma), and six variable interest entities (Affiliates), in which aTyr Pharma, Inc. was considered to be the primary beneficiary (see Note 3). The Affiliates were dissolved in the fourth quarter of 2014. All intercompany transactions and balances are eliminated in consolidation.

Liquidity

The Company has a limited operating history and the revenue and income potential of the Company's business and market are unproven. The Company has experienced net losses and negative cash flows from operating activities since its inception. The Company expects to continue to incur net losses and negative cash flows from operating activities into the foreseeable future. Successful transition to attaining profitable operations is dependent upon achieving a level of revenues adequate to support the Company's cost structure.

The Company plans to continue to fund its losses from operations and capital funding needs through public or private equity or debt financings or other sources. If the Company is not able to secure adequate additional funding, the Company may be forced to make reductions in spending, extend payment terms with suppliers, liquidate assets where possible, or suspend or curtail planned programs. Any of these actions could materially harm the Company's business, results of operations and future prospects.

Use of Estimates

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

Unaudited Pro Forma Balance Sheet Information

The unaudited pro forma balance sheet information as of December 31, 2014 assumes the conversion of all outstanding shares of redeemable convertible preferred stock into 9,238,868 shares of the Company's common stock and the related reclassification of the carrying value of the redeemable convertible preferred stock and warrant liabilities to additional paid-in capital upon completion of the Company's initial public offering (IPO). Shares of common stock issued in such IPO and any related net proceeds are excluded from the pro forma information.

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. The Company views its operations and manages its business in one operating segment.

2. Summary of Significant Accounting Policies

Cash and Cash Equivalents

Cash and cash equivalents consists primarily of readily available checking, money market accounts and money market funds. The Company considers all highly liquid investments that have maturities of three months or less when purchased to be cash equivalents.

Investment Securities

Investment securities primarily consist of investment grade corporate debt securities and commercial paper. The Company classifies all investment securities as available-for-sale and as current assets, as the sale of such securities may be required prior to maturity to execute management strategies. Investment securities are carried at fair value, with the unrealized gains and losses, if any, reported as a component of other comprehensive income (loss) in stockholders' equity (deficit) until realized. Realized gains and losses from the sale of investment securities, if any, are determined on a specific identification basis. A decline in the market value of any investment security below cost that is determined to be other than temporary will result in an impairment charge to earnings and a new cost basis for the security is established. No such impairment charges were recorded for any period presented. Premiums and discounts are amortized or accreted over the life of the related security as an adjustment to yield using the straight-line method and are included in interest income. Interest income is recognized when earned. As of December 31, 2013 the Company had no investment securities. As of December 31, 2014, the Company held $2.0 million of corporate debt securities, all of which mature in less than three months, and there was no difference between the amortized cost and fair value of these investment securities.

Concentration of Credit Risk

Financial instruments that potentially subject the Company to significant concentration of credit risk consist primarily of cash, cash equivalents and investment securities. The Company has established guidelines regarding diversification of investments and their maturities, which are designed to maintain principal and maximize liquidity. The Company maintains deposits in federally insured financial institutions in excess of federally insured limits. The Company has not experienced any losses in such accounts and management believes that the Company is 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 the Company's current and historical operating losses and negative cash flows from operations are indicators of impairment, management believes that future cash flows to be received support the carrying value of its long-lived assets and, accordingly, has not recognized any impairment losses since inception.

Accrued Expenses

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

Deferred Rent

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

Preferred Stock Warrant Liabilities

The Company has issued freestanding warrants to purchase shares of its Series B, Series C and Series D redeemable convertible preferred stock. Since the underlying redeemable convertible preferred stock is classified outside of permanent equity, these warrants are classified as liabilities in the accompanying consolidated balance sheets. The Company adjusts the carrying value of such warrants to their estimated fair value at each reporting date, with any related increase or decrease in the fair value recorded as an increase or decrease to other income (expense) in the consolidated statements of operations. The warrant liabilities will continue to be adjusted to fair value until such time as the warrants are no longer outstanding or the underlying securities are no longer redeemable outside the control of the Company, including at the completion of the IPO.

Research and Development Costs

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

aTyr Pharma, Inc.

Notes to Consolidated Financial Statements—(Continued)

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 grants recognized over the requisite service period of the awards (usually the vesting period) on a straight-line basis, net of estimated forfeitures. For stock option grants with performance-based milestones, the expense is recorded over the service period after the achievement of the milestone is probable or the performance condition is achieved. The Company accounts for stock options granted to non-employees using the fair value approach. These option grants are subject to periodic revaluation over their vesting terms. The Company estimates the fair value of employee and non-employee stock option grants using the Black-Scholes option pricing model.

Income Taxes

The Company accounts 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.

The Company recognizes net deferred tax assets to the extent that the Company believes these assets are more likely than not to be realized. In making such a determination, management considers 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 management determines that the Company would be able to realize its deferred tax assets in the future in excess of their net recorded amount, management would make an adjustment to the deferred tax asset valuation allowance, which would reduce the provision for income taxes.

The Company records uncertain tax positions on the basis of a two-step process whereby (1) management determines 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, management recognizes the largest amount of tax benefit that is more than 50% likely to be realized upon ultimate settlement with the related tax authority. The Company recognizes interest and penalties related to unrecognized tax benefits within income tax expense. Any accrued interest and penalties are included within the related tax liability.

In July 2013, the Financial Accounting Standards Board (FASB) issued guidance that requires an unrecognized tax benefit, or a portion of an unrecognized tax benefit, to be presented in the financial statements as a reduction to a deferred tax asset for a net operating loss carryforward, a similar tax loss, or a tax credit carryforward, unless an exception applies. The guidance is effective for fiscal years, and interim periods within those fiscal years, beginning after December 15, 2013. The Company early adopted this guidance for the year ended December 31, 2013, which is reflected in the financial statements as of and for the year ended December 31, 2013. There was no material impact on the financial statements upon adoption.

aTyr Pharma, Inc.

Notes to Consolidated Financial Statements—(Continued)

Comprehensive Loss

Comprehensive loss is defined as a change in equity during a period from transactions and other events and circumstances from non-owner sources. Net loss and comprehensive loss were the same for all periods presented.

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. The Company has excluded weighted average shares subject to repurchase of 76,587 shares and 61,457 shares from the weighted average number of common shares outstanding for the years ended December 31, 2013 and 2014, respectively. Diluted net loss per share attributable to common stockholders is calculated by dividing the net loss attributable to common stockholders by the weighted average number of common stock equivalents outstanding for the period determined using the treasury-stock method. Dilutive common stock equivalents are comprised of redeemable convertible preferred stock, warrants for the purchase of redeemable convertible preferred stock and options outstanding under the Company's stock option plan. For all periods presented, there is no difference in the number of shares used to calculate basic and diluted shares outstanding due to the Company's 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:

	December 31,	
	2013	2014
Redeemable convertible preferred stock outstanding	9,238,868	9,238,868
Redeemable convertible preferred stock issuable upon conversion of convertible promissory note	94,455	94,455
Warrants for redeemable convertible preferred stock	18,514	25,970
Common stock options	821,057	1,514,471
	10,172,894	10,873,764

aTyr Pharma, Inc.

Notes to Consolidated Financial Statements—(Continued)

Unaudited Pro Forma Net Loss Per Share

The following table summarizes the Company's unaudited pro forma net loss per share (in thousands, except share and per share data):

	Year Ended December 31, 2014 (unaudited)
Numerator:	
Net loss attributable to common stockholders	$ (24,766)
Change in fair value of warrant liabilities	(36)
Accretion to redemption value of redeemable convertible preferred stock	416
Pro forma net loss attributable to common stockholders	$ (24,386)
Denominator:	
Weighted average shares outstanding, basic and diluted	834,221
Pro forma adjustments to reflect assumed weighted average effect of conversion of redeemable convertible preferred stock	9,238,868
Pro forma weighted average shares outstanding, basic and diluted	10,073,089
Pro forma net loss per share attributable to common stockholders, basic and diluted	$ (2.42)

Recent Accounting Pronouncements

In June 2014, the FASB issued ASU No. 2014-10, *Development Stage Entities (Topic 915) Elimination of Certain Financial Reporting Requirements, Including an Amendment to Variable Interest Entities Guidance in Topic 810, Consolidation*. This ASU does the following, among other things: (1) eliminates the requirement to present inception-to-date information on the statements of income, cash flows, and stockholders' equity; (2) eliminates the need to label the financial statements as those of a development stage entity; (3) eliminates the need to disclose a description of the development stage activities in which the entity is engaged; and (4) amends FASB ASC 275, *Risks and Uncertainties*, to clarify that information on risks and uncertainties for entities that have not commenced planned principal operations is required. The amendments in ASU No. 2014-10 related to the elimination of Topic 915 disclosures and the additional disclosure for Topic 275 are effective for public companies for annual and interim reporting periods beginning after December 15, 2014. Early adoption is permitted. The Company has early adopted this new guidance in its consolidated financial statements for the year ended December 31, 2013, and therefore has not labeled its consolidated financial statements as those of a development stage entity or included the previously required inception-to-date information.

In August 2014, the FASB issued ASU 2014-15, *Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern*. ASU 2014-15 requires management to evaluate relevant conditions, events and certain management plans that are known or reasonably knowable that when, considered in the aggregate, raise substantial doubt about the entity's ability to continue as a going concern within one year after the date that the consolidated financial statements are issued, for both annual and interim periods. ASU 2014-15 also requires certain disclosures around management's plans and evaluation, as well as the plans, if any, that are intended to mitigate those conditions or events that will alleviate the substantial doubt. ASU 2014-15 is effective for fiscal years ending after December 15, 2016. The Company is currently evaluating the impact that the adoption of ASU 2014-15 will have on its consolidated financial statements and related disclosures.

aTyr Pharma, Inc.

Notes to Consolidated Financial Statements—(Continued)

3. Affiliates

In October and November 2011, the Company established the Affiliates to perform research and development for specified programs. In April 2012, the Company purchased preferred and common stock of each Affiliate and subsequently issued those shares to each of the Company shareholders in the form of dividends, in proportion to their relative holdings of aTyr Pharma, Inc., in order to effectuate the spin-out of the Affiliates into stand-alone entities. The Company and each Affiliate entered into nonexclusive license agreements allowing each of the six Affiliates to utilize certain intellectual property owned by the Company. The Company and each Affiliate also entered into research and development services agreements in the Company's therapeutic program area of interest covered by the respective nonexclusive license agreement. The working capital of the Affiliates was primarily provided by amounts borrowed from aTyr Pharma, Inc. under convertible promissory note agreements. The Affiliates were not capitalized with sufficient equity to finance their operations and were therefore each considered a variable interest entity, or VIE. In May 2012, the Affiliates commenced operations. The Affiliates have no employees and substantially all of their expenses relate to the services provided to them by aTyr Pharma, Inc. The expenses related to services provided by aTyr Pharma, Inc. are eliminated in consolidation. The liquidation preference structure underlying the preferred stock issued by the Affiliates and the convertible promissory notes issued by the Affiliates to aTyr Pharma, Inc. in exchange for cash effectively protected the Affiliate stockholders from absorbing the losses of the Affiliates and, as a result, no losses were allocated to these noncontrolling interests and such losses were included in the consolidated net loss of the Company. None of the related parties to the Affiliates individually had the power and benefits to control the Affiliates. aTyr Pharma, Inc. is the related party that is most closely associated with the Affiliates and therefore is considered to be the primary beneficiary, and has consolidated the six Affiliates for financial reporting purposes.

In the fourth quarter of 2014, the board of directors and stockholders of each of the Affiliates approved the dissolution of each applicable Affiliate in accordance with the laws of its respective jurisdiction of organization. In connection with the dissolution of the Affiliates, the license and operating agreements by and between aTyr Pharma, Inc. and each Affiliate were terminated. The Company's consolidated financial statements for periods after the effectiveness of the dissolution of the Affiliates no longer include a noncontrolling interest, and the operating activities that the Affiliates performed prior to dissolution will be continued by aTyr Pharma, Inc. The carrying value of the noncontrolling interest was reclassified to the redeemable convertible preferred stock and stockholders' equity (deficit) of aTyr Pharma, Inc. upon dissolution.

From May 2012 through December 2014, the Company provided research and development and management services to the six Affiliates through utilization of its employees, equipment, and facilities. In addition, the Company provided financial support through loans to the Affiliates.

The aggregate carrying amount and classification of the Affiliates' assets and liabilities were as follows (in thousands):

	December 31, 2013
Cash and cash equivalents	$ 1,914
Total assets of Affiliates	$ 1,914
Amounts due to aTyr Pharma, Inc.	$ 12,864
Total liabilities of Affiliates	$ 12,864

aTyr Pharma, Inc.

Notes to Consolidated Financial Statements—(Continued)

The aggregate statements of operations and statements of cash flows of the Affiliates are as follows (in thousands):

	Years Ended December 31,	
	2013	2014
Operating expenses	$(8,856)	$(7,193)
Other expense	(18)	(33)
Net loss of Affiliates	$(8,874)	$(7,226)
Cash used in operating activities	$(8,861)	$(7,193)
Cash provided by financing activities – aTyr Pharma, Inc.	8,047	5,250
Cash provided by financing activities – issuance of common and preferred stock of Affiliates	2,388	29
Increase (decrease) in cash and cash equivalents of Affiliates	$ 1,574	$(1,914)

4. Balance Sheet Details

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

	December 31,	
	2013	2014
Computer and office equipment	$ 364	$ 372
Scientific and laboratory equipment	2,607	2,848
Tenant improvements	1,668	1,668
	4,639	4,888
Less accumulated depreciation and amortization	(2,134)	(2,963)
	$ 2,505	$ 1,925

Accrued expenses consist of the following (in thousands):

	December 31,	
	2013	2014
Compensation and benefits	$1,533	$ 684
Other accrued expenses	1,408	2,248
	$2,941	$2,932

5. 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 the Company for loans with similar terms, which is considered a Level 2 input, the Company believes that the fair value of its commercial bank debt and convertible promissory notes approximate their carrying values. Investment securities and preferred stock warrant liabilities are recorded at fair value.

aTyr Pharma, Inc.

Notes to Consolidated Financial Statements—(Continued)

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 the Company 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 the Company's investments in corporate debt securities and commercial paper. Financial liabilities measured at fair value on a recurring basis include the Company's preferred stock warrant liabilities. None of the Company's non-financial assets and liabilities are recorded at fair value on a non-recurring basis. No transfers between levels have occurred during the periods presented.

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

		Fair Value Measurements Using		
		Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
As of December 31, 2014:				
Assets:				
Corporate debt securities	$1,954	$ -	$1,954	$ -
Liabilities:				
Preferred stock warrant liabilities	$ 319	$ -	$ -	$ 319
As of December 31, 2013:				
Liabilities:				
Preferred stock warrant liabilities	$ 207	$ -	$ -	$ 207

All warrant liabilities are recorded at fair value utilizing the Black-Scholes option pricing model using significant unobservable inputs consistent with the inputs used for the Company's stock-based compensation expense adjusted for the warrants' expected life.

aTyr Pharma, Inc.

Notes to Consolidated Financial Statements—(Continued)

The following table provides a reconciliation of all liabilities measured at fair value using Level 3 significant unobservable inputs (in thousands):

	Warrant Liabilities
Balance at December 31, 2012	$ 42
Issuance of preferred stock warrants	137
Increase in fair value of warrant liabilities	28
Balance at December 31, 2013	207
Issuance of preferred stock warrants	148
Decrease in fair value of warrant liabilities	(36)
Balance at December 31, 2014	$ 319

6. Debt, Commitments and Contingencies

Commercial Bank Debt

Commercial bank debt and unamortized discount balances are as follows (in thousands):

	December 31,	
	2013	2014
Commercial bank debt	$5,000	$ 8,439
Less debt discount, net of current portion	(61)	(60)
Commercial bank debt, net of debt discount	4,939	8,379
Less current portion of commercial bank debt	(781)	(3,237)
Commercial bank debt, net of current portion	$4,158	$ 5,142
Current portion of commercial bank debt	$ 781	$ 3,237
Current portion of debt discount	(53)	(103)
Current portion of commercial bank debt	$ 728	$ 3,134

In each of April 2012 and August 2012, the Company borrowed $1.25 million under a loan and security agreement with Silicon Valley Bank (SVB Loan), at fixed interest rates of 4.89% and 4.85%, respectively. The Company was obligated to make interest-only payments through December 2012 and, beginning in December 2013, equal monthly payments of principal and interest through the maturity date in December 2015. The SVB Loan was amended in July 2013 to increase the available credit under the agreement to $10.0 million. In July 2013, the Company borrowed $5.0 million under the SVB Loan at a fixed interest rate of 5.0% and received $2.9 million of cash proceeds after repayment of the existing principal balance and related accrued interest and fees. In June 2014, the Company borrowed the remaining $5.0 million of available credit at a fixed interest rate of 5.88% and, subsequent to June 2014, had no available credit under the SVB Loan. The Company was obligated to make interest-only payments on each $5.0 million borrowing through June 2014 and, beginning in July 2014, equal monthly payments of principal and interest through the maturity date in June 2017. The final payment due in June 2017 includes an additional fee of $0.5 million, which is being accreted over the term of the debt using the effective interest method and is included in interest expense. The loan is collateralized by all assets of the Company, other than intellectual property, and contains customary affirmative and negative covenants, reporting requirements and events of default.

In July 2013, in connection with the SVB Loan, the Company issued a warrant to purchase 59,312 shares of Series D redeemable convertible preferred stock at an exercise price of $2.529 per share. In June 2014, the

warrant became exercisable for a total of 118,624 shares of Series D redeemable convertible preferred stock when the Company borrowed the remaining $5.0 million of available credit under the SVB Loan. The warrant is fully exercisable and expires on July 24, 2023.

The initial fair value of the warrant in July 2013 was estimated to be $0.1 million and the initial fair value of the additional 59,312 additional warrant shares earned in June 2014 was estimated to be $0.1 million, based on the application of the Black-Scholes option pricing model, and this discount is amortized to interest expense using the effective interest method over the term of the debt.

Future minimum principal and interest payments under the SVB Loan, including the final payment, are as follows (in thousands):

	As of December 31, 2014
2015	$ 3,622
2016	3,622
2017	2,310
	9,554
Less interest and final payment	(1,115)
Commercial bank debt	$ 8,439

Facility Lease

In December 2011, the Company entered into a noncancelable operating lease that included certain tenant improvement allowances and is subject to base lease payments, which escalate over the term of the lease, additional charges for common area maintenance and other costs. The lease expires in May 2017 and the Company has an option to extend the lease for a period of five years. Rent expense for the years ended December 31, 2013 and 2014 was $0.2 million.

In conjunction with this lease, the Company borrowed $2.0 million under a subordinated unsecured convertible promissory note issued to the venture arm of its landlord. The convertible promissory note carries an annual interest rate of 8.0% and matures at the earlier of (i) May 2015, (ii) a liquidation event, or (iii) the closing of an initial firm commitment underwritten public offering of the Company's common stock pursuant to a registration statement under the Act, at which time all outstanding principal and accrued interest amounts would be due, unless previously converted. At any time prior to maturity, the holder may elect to convert the promissory note into shares of the Company's Series D redeemable convertible preferred stock at the price of $2.662 per share. Upon conversion, all then accrued interest will be forgiven. As of December 31, 2013 and 2014, the outstanding principal balance of the convertible promissory note was $2.0 million. As of December 31, 2013 and 2014, the accrued interest on the convertible promissory note was $0.3 million and $0.5 million, respectively.

aTyr Pharma, Inc.

Notes to Consolidated Financial Statements—(Continued)

Future minimum payments under the non-cancelable operating lease as of December 31, 2014 were as follows (in thousands):

	Operating Lease
2015	$ 590
2016	610
2017	231
	$1,431

Research Agreements and Funding Obligations

In October 2007, the Company entered into a research funding and option agreement for certain technologies from The Scripps Research Institute (TSRI). Under the agreement (as amended), the Company provides funding to TSRI to conduct certain research activities. The agreement renews automatically for successive 12 month periods starting on May 31st of each year unless the Company provides 30 days' prior written notice to terminate the agreement. TSRI has the right to terminate the agreement if the Company fails to make any payment under the agreement or for breach or insolvency. Under the research funding and option agreement, TSRI has granted the Company options to enter into license agreements to acquire rights and exclusive licenses to develop, make, have made, use, have used, import, have imported, offer to sell, sell, and have sold certain licensed products, processes and services based on certain technology arising from the sponsored research activities. Pursuant to the terms of these license agreements, TSRI is entitled to receive tiered royalties as a percentage of net sales and a percentage of nonroyalty revenue the Company may receive from its sublicensees or partners, with the amount owed decreasing if it enters into the applicable sublicense or partnering agreement after meeting a specified clinical milestone. In addition, the Company is obligated to pay TSRI up to an aggregate of $2.75 million under each license agreement upon the achievement of specific clinical and regulatory milestone events. A member of the Company's board of directors is a faculty member at TSRI and such payments fund a portion of his research activities conducted at TSRI. For the years ended December 31, 2013 and 2014, the Company recognized expense under the agreement in the amount of $0.6 million and $0.7 million, respectively. The agreement was amended in January 2015 (see Note 10).

During the years ended December 31, 2013 and 2014, the Company provided charitable donations to the National Foundation for Cancer Research of $0.4 million. The Company has requested that the donations be restricted to certain basic research in cancer biology and therapeutics, a portion of which fund research activities conducted at TSRI in the laboratory of a member of the Company's board of directors.

aTyr Pharma, Inc.

Notes to Consolidated Financial Statements—(Continued)

7. Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit)

Redeemable Convertible Preferred Stock

The authorized, issued and outstanding shares of redeemable convertible preferred stock by series were as follows (in thousands, except share and per share amounts):

	Shares Authorized	Shares Outstanding	Liquidation Preference Per Share	Liquidation Preference and Redemption Value	Carrying Value as of December 31, 2013	Carrying Value as of December 31, 2014
Series A	2,925,000	2,925,000	$0.2500	$ 731	$ 731	$ 731
Series B	12,672,000	12,600,000	0.8333	10,500	10,500	10,500
Series B-2	14,686,583	14,686,583	0.8333	12,238	12,238	12,238
Series C	25,015,959	25,000,002	0.9400	23,500	23,500	23,500
Series D	20,473,329	18,275,830	2.6620	48,650	46,196	48,650
	75,772,871	73,487,415		$ 95,619	$ 93,165	$ 95,619

During 2005, the Company sold 2,925,000 shares of Series A redeemable convertible preferred stock at $0.25 per share for gross proceeds of $0.7 million in cash.

During 2006, the Company sold 12,600,000 shares of Series B redeemable convertible redeemable preferred stock at $0.8333 per share for gross proceeds of $10.5 million in cash. The Company incurred $44,000 of offering costs in connection with this stock issuance.

During 2009, the Company sold 14,686,583 shares of Series B-2 redeemable convertible preferred stock at $0.8333 per share for gross proceeds of $12.2 million in cash. The Company incurred $0.1 million of offering costs in connection with this stock issuance.

During 2010 and 2011, the Company sold an aggregate of 25,000,002 shares of Series C redeemable convertible preferred stock at $0.94 per share for gross proceeds of $23.5 million in cash. The Company incurred $0.1 million of offering costs in connection with this stock issuance.

In March 2013, the Company issued convertible notes to investors totaling $10.0 million. The notes carried a 7.0% interest rate. In April and May 2013, the Company sold an aggregate of 18,275,830 shares of Series D redeemable convertible preferred stock for aggregate gross proceeds of $48.7 million, inclusive of the conversion of the convertible notes and related accrued interest and shares of Series D redeemable convertible preferred stock sold by the Affiliates. The Company incurred $0.5 million of offering costs in connection with this stock issuance.

Conversion

The shares of Series A, Series B, Series B-2, Series C, and the Series D redeemable convertible preferred stock (together, the Series Preferred) are convertible into 0.12572 shares of common stock, at the option of the holder. Each share of the Series Preferred is automatically converted into common stock upon either (i) the Company's sale of its common stock in an underwritten public offering pursuant to a registration statement under the Securities Act of 1933, as amended, in which the per share price is at least $42.348 (as adjusted), the net cash proceeds are at least $25,000,000, and the result of offering is listing on a national securities exchange or (ii) upon the majority vote of the holders of Series B-2, Series C and Series D redeemable convertible preferred stock, voting together as a single class, including at least a majority of the Series D stockholders.

aTyr Pharma, Inc.

Notes to Consolidated Financial Statements—(Continued)

Liquidation

The Series D redeemable preferred stock has a liquidation preference of $2.662 per share, plus any declared but unpaid dividends, in priority to the Series A, Series B, Series B-2, and Series C redeemable convertible preferred stock, in which the Series D holders shall receive their full liquidation preference in advance of the other classes of preferred stock. Upon payment of the full liquidation preference of Series D holders, the holders of Series C and Series B-2 redeemable convertible preferred stock are entitled to receive their liquidation preference of $0.94 and $0.8333 per share, respectively, plus any declared but unpaid dividends. Upon payment of the full liquidation preference of Series C and Series B-2 holders, the holders of Series B and Series A redeemable convertible preferred stock are entitled to receive their liquidation preference of $0.8333 and $0.25 per share, respectively, plus any declared but unpaid dividends, prior to and in preference to any distribution of the assets of the Company to common stockholders. The remaining assets of the Company are to be distributed to the common stockholders based on the number of shares of common stock held by each stockholder.

Dividends

The holders of Series Preferred Stock are entitled to non-cumulative dividends at a rate of 8.0% of the purchase price for the applicable series of redeemable convertible preferred stock per share per annum and are payable only if and when declared by the Company's board of directors. The Series Preferred Stock participates in any dividends paid to the holders of common stock on an as-converted to common stock basis. As of December 31, 2014, the board of directors had not declared any dividends.

Redemption

The Series Preferred Stock may be redeemed, in whole or in part, at the option of the holders any time after April 2018, upon the majority vote of the holders of Series B-2, Series C and Series D, voting together as a single class, including at least a majority of the Series D stockholders. The redemption amount is equal to the then current liquidation preference of each share of redeemable convertible preferred stock and is payable in three equal annual installments.

Prior to closing of the Series D redeemable convertible preferred stock financing in April 2013, the redemption amount of the Series Preferred Stock was based on the original liquidation preference of each series of redeemable convertible preferred stock and increased each period at a rate of 10% per annum. The Company recorded the accretion of such amounts as increases to the carrying value of the Series Preferred Stock. In connection with the Series D redeemable convertible preferred stock financing in April 2013, the cumulative increase over the original liquidation preference of the Series Preferred Stock of the Company was eliminated. The Company deemed this change to represent a modification to the Series Preferred Stock which was accounted for as a capital contribution from stockholders who are considered related parties of the Company as they owned approximately 90% of the outstanding capital stock at that date. Accordingly, the resulting adjustment to the carrying value of the redeemable convertible preferred stock was reclassified from mezzanine equity to additional paid-in capital in April 2013.

Voting

The holders of each share of Series Preferred Stock are entitled to one vote for each share of common stock into which the Series Preferred would convert.

aTyr Pharma, Inc.

Notes to Consolidated Financial Statements—(Continued)

Stock Options

The Company 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 grant of 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 the Company's 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 granted under the 2014 Plan is ten years. Options granted prior to September 2012 generally vest over four years and options granted thereafter generally vest over six years. As of December 31, 2014, the Company had 2,039,066 shares authorized for issuance to employees, nonemployee directors, and consultants of the Company under the 2014 Plan.

Stock option activity under the 2014 Plan is summarized as follows:

	Number of Options	Weighted-Average Exercise Price
Outstanding at December 31, 2012	705,661	$ 0.80
Granted	289,237	$ 4.06
Exercised	(67,645)	$ 0.78
Forfeited	(106,196)	$ 0.80
Outstanding at December 31, 2013	821,057	$ 1.95
Granted	753,418	$ 7.21
Exercised	(53,289)	$ 0.83
Forfeited	(6,715)	$ 3.86
Outstanding at December 31, 2014	1,514,471	$ 4.60

Information about the Company's outstanding stock options is as follows (in thousands, except share and per share data):

	Number of Shares	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value
December 31, 2014:				
Options outstanding	1,514,471	$4.60	8.44	$11,905
Options vested and expected to vest	1,514,471	$4.60	8.44	$11,905
Options exercisable	406,933	$1.67	7.06	$ 4,116
December 31, 2013:				
Options outstanding	821,057	$1.95	8.43	$ 1,735
Options vested and expected to vest	778,906	$1.99	8.50	$ 1,594
Options exercisable	255,942	$1.03	7.56	$ 768

Stock-Based Compensation Expense

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,	
	2013	2014
Expected term (in years)	6.52 – 6.56	5.77 – 6.56
Risk-free interest rate	2.0% – 2.2%	1.7% – 2.7%
Expected volatility	109%	111%
Expected dividend yield	-	-

Expected term. The expected term represents the period of time that options are expected to be outstanding. Because the Company does not have sufficient historical exercise behavior, it determines 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. The Company bases 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. The Company bases the expected dividend yield assumption on the fact that it has never paid cash dividends and has no present intention to pay cash dividends.

The allocation of stock-based compensation is as follows (in thousands):

	Years Ended December 31,	
	2013	2014
Research and development	$ 96	$ 527
General and administrative	59	1,264
	$155	$1,791

During the fourth quarter of 2014 the Company modified certain vesting conditions of performance based equity awards for the Company's Chief Executive Officer resulting in incremental share-based compensation costs of $0.7 million, of which $0.6 million was recognized as expense during 2014.

The weighted-average grant date fair values of stock options granted by the Company during the years ended December 31, 2013 and 2014 was $3.42 per share and $10.18 per share, respectively. The aggregate intrinsic value of stock options exercised during the years ended December 31, 2013 and 2014 was $47,000 and $0.4 million, respectively. As of December 31, 2014, total unrecognized share-based compensation costs related to unvested stock options of the Company were approximately $8.0 million. This unrecognized cost is expected to be recognized over a weighted-average period of approximately 4.9 years on a straight-line basis.

aTyr Pharma, Inc.

Notes to Consolidated Financial Statements—(Continued)

Warrants

Information about the Company's outstanding and fully exercisable redeemable convertible preferred stock warrants is as follows:

	Outstanding Warrants		Exercise Price Per Share	Expiration Date
	December 31, 2013	December 31, 2014		
Series B	72,000	72,000	$ 0.8334	September 2017
Series C	15,957	15,957	0.9400	March 2021
Series D	59,312	118,624	2.5290	July 2023
	147,269	206,581		

Common Stock Reserved for Future Issuance

Common stock reserved for future issuance is as follows:

	December 31,	
	2013	2014
Conversion of redeemable convertible preferred stock	9,238,868	9,238,868
Conversion of redeemable convertible preferred stock issuable upon conversion of promissory note	94,455	94,455
Redeemable convertible preferred stock warrants	18,514	25,970
Common stock options granted and outstanding	821,057	1,514,471
Awards available under the 2014 Plan	581,388	180,190
	10,754,282	11,053,954

8. Income Taxes

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

	Years Ended December 31,	
	2013	2014
United States	$ (11,085)	$ (34,885)
Foreign	(8,929)	10,535
	$ (20,014)	$ (24,350)

aTyr Pharma, Inc.

Notes to Consolidated Financial Statements—(Continued)

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,	
	2013	2014
Expected income tax benefit at federal statutory rate	$(6,804)	$ (8,279)
State income taxes, net of federal benefit	(634)	(2,023)
Permanent items and other	2	(321)
Stock-based compensation	-	396
Research credits	(397)	(372)
Unrecognized tax benefits	159	144
Foreign rate differential	2,978	(3,391)
Other, net	(26)	293
Change in valuation allowance	4,722	13,553
Income tax (benefit) expense	$ -	$ -

Deferred income taxes are provided for temporary differences in recognizing certain income and expense items for financial and tax reporting purposes. The deferred tax assets consisted primarily of the income tax benefits from net operating loss (NOL) carryforwards, research and development credits and capitalized research and development expenses, along with other accruals and reserves. Valuation allowances of $21.3 million and $34.8 million as of December 31, 2013 and 2014, 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 the Company's deferred tax assets are summarized as follows (in thousands):

	December 31,	
	2013	2014
Net operating loss carryforwards	$ 13,093	$ 20,066
Capitalized research and development expenses	6,684	7,855
Research credits and other state credits	1,171	1,368
Intangible assets	28	4,926
Depreciation and amortization	(360)	(260)
Reserve and accruals	677	891
Valuation allowance	(21,293)	(34,846)
Net deferred tax assets	$ -	$ -

In the fourth quarter of 2014, the Company dissolved all of the Affiliates and, as a result, acquired intellectual property originally developed by the Affiliates. For book purposes, as this was a transaction between consolidated entities, no intangible asset was recognized. For tax purposes, the intellectual property will be amortized over 15 years resulting in an increase to deferred tax assets as of December 31, 2014. The increase in deferred tax assets was offset by a corresponding adjustment to the valuation allowance. As a result of the dissolution, the Company forgave intercompany loans and recorded a corresponding tax deduction; whereas the Affiliates recognized cancellation of debt income which was offset by net operating losses.

At December 31, 2014, the Company had approximately $47.8 million, $49.7 million, and $5.4 million of net operating loss carryforwards for federal, state, and foreign purposes, respectively, net of Section 382 limitations, available to offset future taxable income. The federal and state net operating loss carryforwards begin to expire in 2025 and 2016, respectively. The foreign net operating losses carry over indefinitely. At

aTyr Pharma, Inc.

Notes to Consolidated Financial Statements—(Continued)

December 31, 2014, the Company had federal and state research and development credit carryforwards of approximately $1.3 million and $1.4 million, respectively, net of Section 382 limitations, which begin to expire in 2026 for federal purposes and carry over indefinitely for state purposes.

Utilization of the domestic NOL and research and development credit carryforwards may be subject to a substantial annual limitation due to ownership change limitations that may have occurred or that could occur in the future, as required by Section 382 and 383 of the Internal Revenue Code of 1986, as amended (the Code), as well as similar state and foreign provisions. These ownership changes may limit the amount of NOL and research and development credit carryforwards that can be utilized annually to offset future taxable income and tax, respectively. In general, an "ownership change" as defined by Section 382 of the Code results from a transaction or series of transactions over a three-year period resulting in an ownership change of more than 50 percentage points of the outstanding stock of a company by certain stockholders. Since the Company's formation, the Company has raised capital through the issuance of capital stock on several occasions which on its own or combined with the purchasing stockholders' subsequent disposition of those shares, has resulted in such an ownership change, and could result in an ownership change in the future.

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

The Company recognizes 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.

The Company's practice is to recognize interest and penalties related to income tax matters in income tax expense. The Company had no accrual for interest and penalties on the Company's balance sheet and has not recognized interest or penalties in the consolidated statements of operations for the years ended December 31, 2013 and 2014.

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

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

The activity related to the Company's unrecognized tax benefits is summarized as follows (in thousands):

Balance at December 31, 2012	$ 774
Increase related to prior year tax positions	79
Increase related to current year tax positions	94
Balance at December 31, 2013	947
Other decreases	(18)
Increase related to current year tax positions	177
Balance at December 31, 2014	$1,106

aTyr Pharma, Inc.

Notes to Consolidated Financial Statements—(Continued)

The Company does not anticipate that the amount of unrecognized tax benefits as of December 31, 2014 will change within the next twelve months.

The Company is subject to taxation in the United States, Hong Kong and state jurisdictions. The Company's 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.

9. 401(k) Plan

The Company maintains 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. The Company, at its discretion, may make certain matching contributions to the 401(k) plan. As of December 31, 2014, the Company had not made any matching contributions.

10. Subsequent Events

The Company has completed an evaluation of all subsequent events through April 3, 2015 to ensure that this filing includes appropriate disclosure of events both recognized in the December 31, 2014 consolidated financial statements and events which occurred but were not recognized in the consolidated financial statements. Except as described below, the Company has concluded that no subsequent event has occurred that requires disclosure.

Amended Research Funding and Option Agreement and Assignment Agreement

In January 2015, the Company and TSRI entered into an amended and restated research funding and option agreement pursuant to which the Company agreed to issue 119,840 shares of its common stock to TSRI for a purchase price of approximately $0.008 per share in consideration for the adjustment of sublicense payments and the assignment of certain intellectual property rights by TSRI to the Company. The Company issued the shares of common stock to TSRI on March 31, 2015.

Increase in Shares of Common Stock Reserved for Issuance under the 2014 Plan

On January 1, 2015, the number of shares of common stock reserved for issuance under the 2014 Plan increased from 2,039,066 shares to 2,445,019 shares as a result of the evergreen provisions of the plan. On March 31, 2015, the Company's board of directors and stockholders approved an increase in the number of shares of common stock reserved for issuance under the 2014 Plan from 2,445,019 shares to 3,480,079 shares.

Amended and Restated Certificate of Incorporation

On March 30, 2015, the Company amended and restated its certificate of incorporation to, among other things, (1) increase its authorized shares of common stock from 95,500,000 to 185,000,000 shares, (2) increase its authorized shares of preferred stock from 75,772,871 to 143,939,765 shares, of which 68,166,894 shares are designated as Series E preferred stock, and (3) set forth the rights, preferences and privileges of the Series E preferred stock.

Sale of Series E Redeemable Convertible Preferred Stock

On March 31, 2015, pursuant to a Series E stock purchase agreement, the Company issued an aggregate of 68,166,894 shares of its Series E redeemable convertible preferred stock at a purchase price of $1.119 per share, for aggregate cash consideration of $76.3 million. Each share of Series E redeemable convertible preferred stock

is convertible into 0.12572 shares of the Company's common stock. If the Company completes a qualified public offering on or before March 1, 2016, each share of Series E redeemable convertible preferred stock would convert into approximately 0.10329 of a share of common stock. A qualified public offering must result in listing on a U.S. national securities exchange and at least $50 million of gross proceeds at a per share price of not less than $13.00.

March 31, 2015 and April 2, 2015 Stock Options

On March 31, 2015 and April 2, 2015, the Company granted options to purchase an aggregate of 300,280 shares of common stock to employees, board members and consultants at an exercise price of $9.15 per share.

April 17, 2015 and April 25, 2015 Stock Options

On April 17, 2015, the Company granted options to purchase an aggregate of 282,868 shares of common stock to members of the Company's executive team at an exercise price of $9.15 per share. In addition, the Company's board of directors approved options to purchase an aggregate of 377,158 shares of common stock to such members of the executive team at an exercise price equal to the initial public offering price. These stock options are contingent upon the effectiveness of a registration statement on Form S-1 relating to an IPO that (i) results in at least $50 million of gross proceeds, (ii) is completed on or prior to September 30, 2015 and (iii) meets the definition of a qualified public offering as specified in the Company's amended and restated certificate of incorporation described above. On April 25, 2015, the Company granted options to purchase an aggregate of 56,471 shares of common stock to employees and consultants at an exercise price of $9.15 per share.

Approval of 2015 Plan

On April 25, 2015, the Company's board of directors adopted, and the Company's stockholders approved, the Company's 2015 Stock Option and Incentive Plan (the 2015 Plan). The 2015 Plan will become effective upon the effectiveness of this registration statement. A total of 1,574,566 shares of the Company's common stock will be initially reserved for issuance under the 2015 Plan. In addition, the number of shares reserved and available for issuance under the 2015 Plan will automatically increase each January 1, beginning on January 1, 2016 and thereafter until January 1, 2019, by the lesser of (i) 1,840,000 shares, (ii) 4% of the outstanding number of shares of the Company's common stock on the immediately preceding December 31 or (iii) an amount determined by the Company's board of directors.

Approval of the Employee Stock Purchase Plan

On April 25, 2015, the Company's board of directors adopted, and the Company's stockholders approved, the Company's 2015 Employee Stock Purchase Plan (the 2015 ESPP). The 2015 ESPP will become effective upon the effectiveness of this registration statement. A total of 227,623 shares of the Company's common stock will be initially reserved for issuance under the 2015 ESPP. In addition, the number of shares reserved and available for purchase under the 2015 ESPP will automatically increase each January 1, beginning on January 1, 2016 and thereafter until January 1, 2019, by 1% of the outstanding number of shares of the Company's common stock on the immediately preceding December 31 or such lesser number of shares as determined by the Company's board of directors.

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Notes to Consolidated Financial Statements—(Continued)

Reverse Stock Split

On May 5, 2015, the Company filed an amendment to its amended and restated certificate of incorporation to effect a one-for-7.95413 reverse stock split of the Company's common stock (the Reverse Stock Split). The par value and the authorized shares of the common and convertible preferred stock were not adjusted as a result of the Reverse Stock Split. All issued and outstanding common stock and the conversion ratio of the redeemable convertible preferred stock have been retroactively adjusted to reflect this Reverse Stock Split for all periods presented.

5,360,000 Shares

Common Stock

J.P. Morgan **Citigroup**

BMO Capital Markets

William Blair

May 6, 2015

Through and including May 31, 2015 (the 25th day after the date of this prospectus), all dealers effecting transactions in these securities, whether or not participating in this offering, may be required to deliver a prospectus. This delivery requirement is in addition to the obligation of dealers to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.